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SCIENCE & TECHNOLOGY

USSR: SPACE BIOLOGY & AEROSPACE MEDICINE

VOL 21, NO 5, SEPTEMBER-OCTOBER 1987

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CONTENTS

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MEDICAL AND PSYCHOLOGICAL PROBLEMS OF ASSURING FLIGHT SAFETY UNDER PRESENT CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 12 Mar 87) pp 4-10

[Article by S. A. Bugrov and V. A. Ponomarenko]

[English abstract from source] At the present time flight safety can be provided only if aviation medicine requirements are taken into consideration. Maintenance of good health, high performance and professicnal longevity of the flight and ground crewmen requires that flight surgeons and aerospace medicine specialists revise their position and eliminate various shortcomings in their work. Those latter include: lack of data about correlations between health problems and decline of performance, risk factors and professional longevity; inadequate use of systemic analysis for evaluating man-machine interactions; low priority of the investigations needed to organize proper prophylaxis of diseases. The paper discusses proposals and suggestions with respect to the new types and methods of medical support of flight safety at the current and advanced levels of development of aviation technology.

[Text] Active mental restructuring with respect to interpretation and implementation of new and extremely important tasks put by the 27th Party Congress is one of the key elements in today's public life of aviation physicians and scientists involved in aerospace medicine. We should mention the organic link between new social programs (including the one on social justice) and the problem of inflight crew and passenger safety. In this case, we are referring to intensification of the humanistic component of science, its movement away from the sphere of pure professionalization. As validly noted by I. T. Frolov, today's social practice requires that science be integrated with overall cilture, synthesis of professionalization and humanistic values [10]. As for aviation medicine, its inception is practically related to the most human goal: that of assuring the safety of man in an aircraft, preserving health, work capacity and professional longevity [2].

In the political report of the CPSU Central Committee at the 27th Party Congress, it was noted that the health problem must be viewed from a broad social vantage point. It is determined primarily by living and working conditions. In this light, the problem of flight safety is organically linked with the human factor, and for this reason there is every justification for referring it to the category of morality. There is no doubt that the concept of "morality" has always been an element of aviation medicine. It is expressly the scientists specializing in medical aspects of accidents (N. M. Dobrotvorskiy, V. M. Streltsov, S. Ye. Mints, Ye. S. Kogan, I. K. Sobennikov, S. G. Gellershteyn, K. K. Platonov, A. G. Shishov, P. K. Isakov, F. D. Gorbov, V. A. Popov, A. M. Pikovskiy and others) who founded the ideology of humanism in the practice of medical support of flights, having directed research not only toward development of man's psychophysiological capacities, but elaboration of protective equipment with consideration of his limitations.

It is known that, at the early stage of its development, aviation medicine selected as its key point in assuring flight safety the habitat which, in essence, is the main condition for human life and work capacity. From this originated the main directions of research: elaboration of physiological and biological bases of adaptation to an unusual habitat and establishment of the patterns that control processes of interaction between the environment and the body. The method of simulating negative flight factors was developed for investigation of these matters: hypoxia, impact and radial accelerations, angular accelerations, vibration, heat, etc. Accordingly, equipment was developed to simulate the physical living conditions: altitude chambers and centrifuges, ejection devices, heat and vibration units. Using the modeling method, scientists validated the physiological range and levels of the body's compensatory capacities as related to extreme factors; they established the stages and structures of physiological adaptation, validated the types and composition of protective gear for crews that would assure their work capacity. This indicates that aviation medicine, even at that time, was organically interwoven in diverse aspects of development and operation of aircraft equipment and medical support of pilots' work. History clearly illustrates the vital link between aviation medicine theory and practical medical assurance of flight safety. It is expressly the establishment of organizational bases for introduction of research results that enabled aviation physicians to reduce to a minimum the professional nosology as a disqualifying factor, with all the diversity of professional hazards to which crews are exposed. These positive advances were made thanks to the efforts of scientists--those who organized the medical service in aviation and pedagogues, such as A. P. Popov, A. N. Babiychuk, N. M. Rudnyy, K. F. Borodin, A. V. Pokrovskiy, Yu. M. Volynkin, S. A. Gozulov, O. G. Gazenko, Ye. A. Karpov, P. I. Kaktysh, M. P. Brestkin, A. G. Shishov and others.

Technological progress in aviation compelled aviation medicine not only to constantly learn new investigative methods, but to basically update methodology which, of course, is related to a fragile tradition. Engineering psychology began to develop in the womb of aviation medicine starting in the 1970's, and systems analysis of flight work was adopted. The scientists shifted their attention from reactions of the body to integral performance during man's interaction with equipment. Systems analysis, which discloses the true causes of achievement and failure in performing assigned tasks, became the methodological guideline in studying the efficiency and reliability of

crew performance. Systems analysis consisted in essence of assessing each element of the pilot-aircraft-environment (gear, cabin microclimate, visibility, information system, etc.) system from the standpoint of its contribution to the end result achieved by the crew, in studies of flight safety [3]. It should be stressed here that this methodology is an objective necessity, due to the scientific and technological revolution in aviation. The first thing that technological progress brought was the use of aviation under conditions that were not inherent to it previously, to augment the diversity of special tasks.

The second distinction of technological progress is the dramatic increase in automation. From the psychophysiological point of view, this lead to a change in flight work. Accordingly, new problems arose, which had not been posed before: development and validation of guidelines for coordination of man and automatic equipment, development of means of maintaining a high level of readiness to switch to manual control. It was necessary to theoretically develop the physiological validation for distribution of functions between man and machines. Finally, technological progress brought with it some new hygienic problems, since the increasing power of engines and radar, as well as improved aerodynamic properties of flight vehicles were dialectically inseparably linked with appearance of new occupational hazards in diverse combinations. Here, we should stress one basic distinction: technological progress unexpectedly disclosed that aviation medicine had lost its anticipatory, preventive hygienic role as a social impetus. Some of the research began after the appearance of "sore points" in practice. This was attributable to the fact that technological progress, providing comfortable working conditions, obscured some of the long-term sequelae. This is why it became an urgent neeed to develop, under current conditions, a new scientific strategy, a strategy of anticipatory research in order to prepare in advance for the prevention of accidents. Timely prevention is a scientific methodology that alters appreciably the view of aviation medicine. We refer to involvement of aviation medicine in the process of developing and testing aviation equipment. It is in this new capacity that our science is expected, in the interests of medical support of flight safety, to form a scientific forecast with respect to introduction of future equipment with consideration of the human factor. All this meant that the forecast covers instruction and training, work capacity and health, scope and type of protection against enviornmental hazards. Such an approach of systemic anticipatory research required elaboration of new organizational guidelines. One of them was development of a new form of scientific research--medicopsychological ergonomic elements accompanying aviation equipment that is being developed [1, 3, 4].

The medicopsychological elements of developing the means and conditions of professional activity refer to a set of scientific organizational measures aimed at introduction of the ideology of aviation medicine, in particular, implementation of hygienic, ergonomic and medical-technical specifications for all elements of the man-machine system. The systems approach was the methodology for this type of medical support of the human factor.

The purpose of medicopsychological concomitance is to provide conditions and work tools for pilots that preserve professional health and work capacity, permit attaining a high level of professional reliability. This form of

scientific assurance of flight safety provides for enhancement of reliability and achievement of the human factor. It is expressly the problem of the human factor in interaction with machines that stimulated revision of the content of the science of aviation medicine. It should be stressed once more that concrete analysis of the status of the problem of assuring flight safety is what led to this restructuring of the traditional view of the role of aviation medicine. A tendency was discovered toward divergence between the high level of complexity of aviation equipment, control systems, computer engineering and radio electronics to be assimilated by man and insufficient consideration of the psychophysiological patterns in mental performance and behavior of man when designing working conditions and equipment. As a result, a new phenomenon is revealed, which is not evident to the naked eye--materialization of insufficient knowledge about man in equipment, during operation of which there is consistent decline in reliability of actions. This explains, to some extent, the problem of inadequate efficacy of measures to assure flight safety. Hence it can be concluded that the human factor, in the presence of acceleration of technological progress, emerges to aviation medicine first as a problem of medical and social support of future activities of aviation specialists and, in the second place, as a gauge of the level of permissible complexity of aviation equipment. If such interpretation of the problem of human factor is assimilated in the future by those who design aviation equipment, we can expect that acceleration of technological progress would lead to actual improvement of flight safety level, which is provided in all systems of a manned flight vehicle. The role of the system of medical assurance of flight safety, which organizes anticipatory measures dealing with both new forms of psychophysiological training and strict consideration of observance of hygienic standards of working conditions, is clearly evident in this key point--implementation of interaction between man and machines. The new tasks that arose for aviation medicine were a powerful impetus for development of a new experimental base in the form of models, simulator-model complexes based on a branched computer network.

Without dwelling on the technical aspects, we deem it expedient to describe the current medico-technical ideology of making use of technological progress in the interests of medical support of flight safety. Interaction of crews with newly developed equipment is used on such complexes. The new aspect in methodology of aviation medicine consists of the possibility of preserving mental and physical healthy by means of early medical monitoring of the tools to be used in the future by aviation specialists. Two principles ensue from this: 1) aviation medicine has come close to developing a new theoretical platform--early prevention of accidents--and 2) medicopsychological support of the human factor at the stage of development and testing of aviation equipment implies addition to the technological cycle of developing an aircraft of a stage of engineering psychological half-scale models of upkeep and conditions of perforing professional work. Simulator-model complexes are the tangible execution of formulated ideas. These complexes are a new tool in the hands of scientists--physicians, hygienists, physiologists and psychologists--which enables them to actively penetrate into all levels of the life cycle of a flight vehicle. As an example, let us discuss some of these levels.

At the first level, the extent of implementation of the tactical-technical specifications for equipment and crew's workplace is tested, with consideration

of the human factor, and suggestions are elaborated for adoption of medical recommendations.

At the second level, a physiological and hygienic assessment is made of the workplace during actual professional activity. The simulated new working conditions are instrumental in development of new methods of clinical and physiological evaluation of work capacity, new means of maintaining the psychophysiological state and means of rehabilitation.

At the third level, special-purpose ergonomic programs are elaborated to assess consideration of the human factor during state trials, as well as psychological pedagogic recommendations for instruction and assimilation by flight personnel of the new work tools.

Thus, we are dealing here with development of technical support of aviation medicine that would permit solving problems on a higher level, such as, for example, validation of the technical expediency of levels of complexity which, from the medical point of view, means that equipment is not allowed to exceed the limits, beyond which its successful operation is obtained at the price of health problems. On the basis of this conception, one can formulate tasks for aviation medicine, performance of which is the genuinely scientific contribution of aviation physicians to the social policy of accelerating technological progress. As applied to current conditions, the following should be included among such tasks:

Forecasting efficiency of crew actions

Validation of dynamic physiological and hygienic standards for work places, microclimate, habitat, that are compensated by man without detriment to health

Determination of psychophysiological simulators for formation of a high level of adaptive and compensatory mechanisms of regulating vital functions

Validation of medical suggestions for developing life-support equipment with consideration of the nature of the professional tasks

Thus, establishment of a new scientific experimental foundation for the study of the human factor in interaction with machines is, at the present stage of development of aviation, not only a technical, but social task.

Some of the theoretical views expounded above concerning aviation medicine as a science from the standpoint of assuring flight safety are, of course, debatable, and require participation of a wide range of specialists in discussing them. But there are some "sore points" in today's practice of medical support of flights that require immediate and effective intervention. We are not referring to morbidity as such (it happens to have a tendency to decline), but to reduction of professional reliability of actions (without worsening of health) due to low resistance to occupational hazards in individuals with partial insufficiency of health status. The exceptional psychological stress of performance, even when a landing approach is automated, particularly with 40×400 weather minimum, emerges as the triggering factor. At the present

time, science and practice have established a firm link between manufacture-caused deleterius factors in the habitat, age and morbidity, particularly the type that emerges as a disqualifying factor. Evidently, such facts are the first signs of defending the system of dynamic monitoring of health status that was established and had proven itself for a long time. In our opinion, evaluation of an individual's fitness for flight on the basis of dynamics of some nosology or other is no longer adequate. Evidently, the redirection toward assessing the functional state of of so-called psycho-physiological readiness, which has begun in aviation medicine, with due consideration of current reserve capacities, is the scientific direction that best meets the conditions of scientific and technological progress in aviation [1, 6, 9, 11].

It is not by chance that prenosological diagnostics, dynamic hygienic standard-setting and elaboration of field methods of assessing enzyme, hormone and immunological status got a "shot in the arm" from research in aviation medicine [5]. However, for such a change in scientific direction to become a practical need (in both medicine and organization), it is necessary to elaborate broader theoretical conceptions of health. We consider it a productive idea to develop a new conceptual system concerning habitat and occupational health [8].

What is the substance of the new conceptions?

In the first place, there is elimination of compartmentalization from aviation medicine, since it caused a rigid barrier: the concepts of work capacity, health and disease had virtually no bearing on behavior, professional performance and instruction. As for assuring man's inflight safety, such a situation made it difficult to develop the systems analytic approach. The fact of the matter is that when solving the problem of flight safety, one is governed by concepts such as reliability of the pilot-aircraft-environment system. In this case, reliability should be defined as the probability of achieving a specified result without detriment to human health and life and with preservation of the aircraft. If we consider that environment was the principal object of investigation in aviation medicine, it should not presently be viewed solely as a means of survival. With regard to assuring flight safety, environment is construed as the set of physical and psychological factors that affect the pilot in the course of his interaction with equipment and which alter reliability and efficiency of the entire pilot-aircraft-environment system. Such content of the inhabited environment also includes the information environment and, consequently, informational interaction. The latter, being a regulator of man's mental activity when he controls an aircraft, should become an organic element of aviation medicine (psychohygiene). The future will show that many neurotic reactions and the neurotic genesis of cardiovascular disorders proliferated expressly because of information-related disturbances in man's communication with machines, and this requires inclusion of the problem of "information neuroses" in the realm of concerns of aviation medicine. Technological progress and medical assurance of flight safety compel us to render informational interaction between man and machine a full-blooded object of research in aviation medicine.

Thus we are coming close to the main issue, namely the fact that, under conditions of technological progress, the preventive role of aviation medicine amounts to transfer of the center of gravity from responses of the body to reliability of the human factor, which combins both health and performance. We view this as the new scientific platform of medical support of flight safety. We are referring not only to preservation of health as such, but providing for professional health. The latter is the capacity to retain specified compensatory and defense properties of the body that provide for efficiency under all of the conditions under which professional activity takes place. The concept of professional health, unlike the conventional definition of health, implies the existence of a trait such as the body's capacity to restore an impaired state in accordance with the regulations for volume and type of professional work. With such formulation of the question, we are linking more firmly preservation of health with all elements of the service of assuring flight safety, rather than only the medical one. Hygienic conditions, which emerge as health risk factors, acquire deeper meaning, since they are transformed into the cause of conditions that lower reliability of actions. Thus, everything that threatens professional health also holds a direct threat to flight safety.

The conception of professional health as a risk factor of flight safety will strengthen appreciably realization of the need for an individual approach to planning flight work loads, steps for restoring the functional physical and mental status. Thus, it will be possible to depart from declaration of safeguarding health to a more specific one, restoration of work capacity by a specific flight day. Of course, this stimulates development of new approaches to diagnosis of fatigue, mental demobilization, nervous depletion and other states often encountered among flight personnel. Evaluation of psychophysiological readiness of an individual for specific flight assignments will enhance the role of the flight surgeon and render him a full participant in implementation of tasks performed by flight personnel.

The last thing we must mention in discussing medical support of flight safety is objectivization and social justice in establishing the true causes of flight accidents. Apparently, there is no need to prove that flight safety is also a moral problem, because one should always separate the disaster from blaming the crew when making an investigation. An accurate assessment of physical condition and understanding of the laws of mental activity will help aviation medicine make a more objective determination of the cause of unreliability of the human factor. For this reason, technological progress in aviation should be used in two directions: 1) the accident recorders should define not only movement of the aircraft and condition of its main systems, but the condition of the entire physical environment that affects crew performance; 2) the onboard digital complexes should also have a "human module," i.e., a system of sensors and converters with which the environment and all protective gear providing for optimum performance are controlled. We view this as sociologization of technological progress, which provides the conditions for enhancing performance of the human factor.

The above views and suggestions concerning some new forms and means of medical support of flight safety are viewed as a scientific lever, with which it will be possible to rapidly bring science closer to practice. Implementation of

of an active scientific position for aviation medicine would be helpful in obtainung social programs of assuring the welfare of workers. As applied to aviation, such a position instills hope that the human factor, in the practice of assuring flight safety, will change from a constant threat to flight safety (60-70%) to a gauge of efficiency of the man-machine system.

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EFFECT OF SPACEFLIGHT FACTORS ON PRIMATE'S BLOOD CIRCULATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 17 Feb 87) pp 10-13

[Article by S. V. Abrosimov, V. V. Zhidkov, D. K. Endeka, V. I. Lobachik, V. I. Korolkov and Ye. A. Ilyin]

[English abstract from source] Using radioactive isotopes, central, peripheral and organ blood circulation was investigated in two rhesus monkeys before the 7-day space flight, 1.5 hours after touchdown, and 4 months after recovery. Blood distribution and shifts were measured in different body segments, viz. head, chest, abdomen, legs. Postflight measurements revealed a decrease of plasma and blood volume. They also demonstrated changes in cardiac output and stroke volume, decrease of total peripheral resistance, reduction of mean arterial pressure and a slight increase of heart rate. Pulmonary blood flow velocity and time varied insignificantly and in a different manner. Blood was pooled in the legs. Blood flow velocity in the skin of the upper and lower body decreased while in muscles it increased above the baseline values. Postflight, muscles acted as a hemodynamic blood pool. The tolerance of both monkeys to the tilt test was satisfactory. It can be concluded that the monkeys tolerated the 7-day space flight well enough.

[Text] Soviet and American investigators have demonstrated convincingly that one of the most important findings among the physiological changes observed during spaceflight is functional change in the circulatory system [1-3, 6, 7]. Evidently, weightlessness does not have an appreciable effect on the condition or function of isolated cells [5, 8]. This stresses once more the significance to the body of changes in circulatory homeostasis, which is called upon to provide for the correlation between cellular structures, organs and systems. The body adjusts to weightlessness, forming a new circulatory homeostasis. However, the mechanisms, routes and time of such adaptation have remained undetermined to this time. There are some difficulties involved in conducting a broad integrated study of the cardiovascular system of man during spaceflights are immediately after them at the present time. Experiments with animals conducted aboard biological satellites of the Cosmos series can make a significant contribution to solving this problem.

We shall discuss here the results of testing two monkeys flown for 7 days aboard Cosmos-1667 biosatellite. Our objectives included the following: quantitative assays of blood and plasma volumes and packed red blood cells; investigation of parameters of central, peripheral and organic hemodynamics; examination of quantitative characteristics of regional (head, chest, abdomen, lower extremities) distribution of blood at rest and during functional tests.

Methods

We used essentially radiotracer methods with the following isotopes: ^{131}I-albumin (single dose of up to 0.012 MBq/kg), ^{113m}In-citrate (single dose 0.12 MBq/kg), ^{99m}Tc with pyrophosphate (single dose up to 0.12 MBq/kg) and ^{133}Xe (single dose 0.18 MBq/kg).

A special flight version of a table for radiometry of the monkey's entire body and its different regions was developed [5] to obtain quantitative data on distribution and migration of blood in primates.

The monkeys were examined in the baseline period, 1.5 h after the spaceflight and at the end of the 4th month of the recovery period.

Results and Discussion

The baseline examination revealed that most of the above functions were in the range of the physiological norm inherent in animals of the same age and weight. However, it should be noted that blood, plasma and particularly packed red cell volumes were below the mean-group values of control animals (back-ups) in both animals in the preflight period. The low baseline level of the erythrocyte pool in both monkeys, particularly the one named Gordyy [proud], could be due to a number of causes, among which the most significant one was referable to the medical preventive measures with use of antibiotics of the levomycetin class (Figure 1).

Postflight examination of the monkeys was performed within the first 1.5 h at the landing site. After touchdown, there was insignificant decrease in weight of the monkey named Vernyy [loyal], mainly due to decrease in lean body mass. In the second monkey, while body weight increased in flight (to 140 g), lean mass decreased by 42 g. The amount of blood in the vascular system diminished by 3.1 and 2.2% in Vernyy and Gordyy, respectively. These changes were referable to plasma, which should a 9.4 and 6.8% decrease, respectively. Packed red cell volume was higher postflight than in the base period in both monkeys.

Radiocardiographic tests performed at the landing site revealed different cardiovascular responses to the factors involved in the 7-day spaceflight (see Table). Thus, resting heart rate was 24% faster than preflight in Vernyy. Cardiac output remained virtually at the baseline level, with 18% decrease in stroke volume of the heart. The noted functional central hemodynamic changes occurred in the presence of 8% decline in total peripheral resistance and 5% decline of mean arterial pressure. The observed functional changes in the circulatory system should apparently be interpreted as one of the variants of animal adaptation to the set of spaceflight factors, including accelerations during descent of the spacecraft and acute response to readaptation to earth's gravity. Volumetric flow in the pulmonary circulation and linear blood flow

in the left heart-head segment, which did not change during the flight, are indicative of the compensated nature of the above changes.

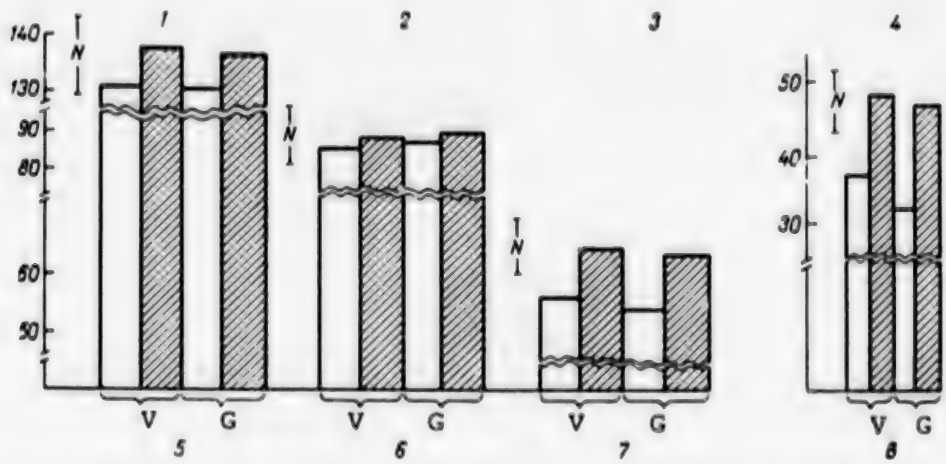

Figure 1. Volumetric parameters (mℓ/lean body mass) of blood for Vernyy and Gordyy in the preflight and recovery (4 months) periods

1) circulating blood volume
2) circulating plasma volume
3) circulating red cell volume
4) venous hematocrit
V) Vernyy
G) Gordyy
N) range of "normal" values in "back-up" group (n = 6)

White bars--preflight, hatched--recovery period

Central and peripheral hemodynamic parameters of monkeys before and after 7-day flight

Name of monkey	Testing time	CO, ℓ/min	SV, mℓ/beat	PFT, s	BV_L, mℓ	TPR, dyne·cm·s^{-5}	BP_m, mm Hg	HR/min	Blood flow time in heart-head, s
Vernyy	Baseline	0,5	3,3	4,36	25	1610	100,7	153	7,25
	Postflight	0,51	2,7	4,35	26	1480	95,6	190	7,0
Gordyy	Baseline	0,61	3,2	3,75	39	1365	99,8	190	6,75
	Postflight	0,78	3,7	3,25	41	1070	96,5	210	6,0

Key: CO) cardiac output
SV) stroke volume
PFT) pulmonary blood flow time
HR) heart rate
BV_L) lung blood volume
TPR) total peripheral resistance
BP_m) mean arterial pressure

Gordyy's circulatory responses to the same factors were somewhat different. While total peripheral resistance of vessels declined, cardiac and stroke output increased by 28 and 16%, respectively. Heart rate was 11% higher than the baseline, there being a 3% decline in mean arterial pressure. Such functional change in central hemodynamics caused some acceleration of blood flow

in the pulmonary circulation and in the left heart-head segment of the arterial system. This type of adaptation of circulatory function is aimed at increasing blood flow in vessels with diminished peripheral resistance.

The results of quantitative evaluation of the process of distribution of blood in monkeys after landing may be of some interest. In our opinion, this feature of circulatory homeostasis not only offers an expert assessment of the vascular collecting system of circulation, but, to some extent, reflects the residual blood redistributing response after being exposed to weightlessness.

Quantative measurements of blood distribution in resting animals (in recumbent position) revealed that it changed postflight in virtually the same direction in both monkeys. Thus, there was 73.5 to 78% decrease in delivery of blood to the thorax postflight, as compared to the baseline in both animals. Blood content in the abdominal region increased by 14 and 3.0% in Vernyy and Gordyy, respectively. The animals showed dramatic increase in delivery of blood to the lower extremities, constituting 135 and 199%, respectively, of baseline values.

In view of the fact that the method used under these conditions offers information about overall blood content in all tissues of a region that are within the visual field of a detector, additional studies were made in order to pinpoint the contribution of different tissues to total blood content in a specific region. For this purpose, we examined the volumetric characteristics of pulmonary blood flow. The results of these studies revealed that there was no inflight change in blood volume in the lungs or circulation time in Vernyy; consequently, the delivery of blood to the lungs remained at the baseline level. In the second monkey, pulmonary circulating blood volume was 5% higher after the flight than in the baseline; however, there was 13% increase in its velocity in the pulmonary circulation, which also could not make an appreciable contribution to the above-mentioned changes in delivery of blood to the thorax.

Studies of volumetric blood flow in the skin and muscles of bipolar body zones revealed significant change.

Thus, blood flow in the skin of the upper and lower halves of the body was 65 and 40% lower than the baseline in Vernyy and Gordyy, respectively. After the flight, both monkeys showed an increase in volumetric blood flow in muscles of the upper extremities and particularly in the lower ones (to 142 and 164%, respectively).

Thus, we demonstrated postflight redistribution of blood, not only among regions, but among different tissues. A study of hemodynamic function would be incomplete without using a functional load. We used an orthostatic (70° for 10 min) and antiorthostatic (-15° tilt, 5 min) tests in this capacity. The test was performed on the above-mentioned radiometric table, with continuous recording of the process of blood migration in the animals. Postflight tolerance to the orthostatic test was quite satisfactory in both monkeys. However, the nature of redistribution of blood during the test changed after the flight (Figures 2 and 3). In the baseline period, blood shifted from the upper half of the body (head, chest) to the lower half, mainly to the lower extremities, in both monkeys during the orthostatic test. After the flight, due to the increase in blood content of lower limb muscles, its migration was

slower in this region in Vernyy, during the orthostatic test, although in general the direction and volume of shifted blood were similar to baseline values. In Gordyy, due to even greater increase in blood content of lower-limb muscles under the influence of gravity during the orthostatic test it moved to capacitive vessels of the abdominal cavity. We consider this change in nature of shifting of blood as an objective sign of worsening of postural stability.

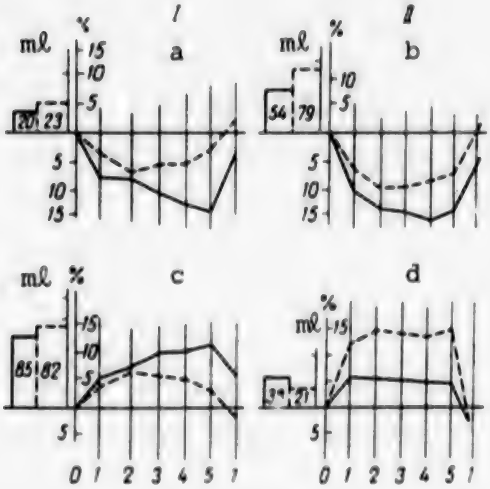

Figure 2.
Nature of shift in plasma during orthostatic test on Gordyy (% of baseline level). X-axes, duration of test (min); arroheads indicate recumbent position

a) head
b) chest
c) abdomen
d) lower extremities
I) preflight
II) postflight

Baseline regional plasma volume (mℓ) given to left of graphs

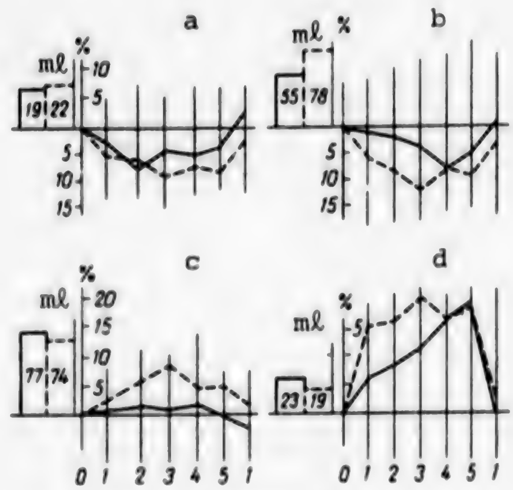

Figure 3.
Nature of shift in plasma during orthostatic test on Vernyy (% of baseline level)

Designations are the same as in Figure 2.

It should be noted that there was appreciable decrease in postflight response of the circulatory system to the tilt test according to extent of migration of blood to the upper half of the body in both monkeys. Evidently, exposure to hypogravity had some conditioning effect on compensatory mechanisms involved in regulating gravity-related migration of blood in a cranial direction. Investigation of parameters of linear blood flow in cereoral vessels using gamma-encephalography postflight failed to demonstrate appreciable deviations from the results of the baseline test. Examination of the animals 4 months after the flight revealed complete normalization of blood circulatory function.

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INFLIGHT SIMIAN CIRCADIAN RHYTHMS AND TEMPERATURE HOMEOSTASIS ABOARD COSMOS-1514 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 16 Dec 86) pp 14-18

[Article by V. Ya. Klimovitskiy, A. M. Alpatov, F. M. Sulzman, C. A. Fuller and M C. Moore-Ede (USSR and United States)]

[English abstract from source] In the course of a 5-day space flight of two rhesus monkeys the following parameters were recorded at an interval of 16 min: core body temperature (Tc), skin temperature (Ts), and motor activity (MA). The telemetric Tc sensor was implanted subcutaneously in the right axilla, Ts thermistor was attached to the right ankle, and the MA piezotape was fixed to the inner side of the vest. Circadian rhythms of Tc varied with a period of 24 hours in one monkey and 25 hours in the other. The daily Tc decreased on the average by 0.5°C, Ts fell immediately after launch and remained close to the lower limit throughout the flight. The Ts amplitude decreased 5-fold. Phases of the circadian rhythms of Ts changed and circadian rhythms of MA remained unchanged and equal to 24 hours.

[Text] The importance of biorhythmological studies in space is attributable to the fact that expected changes in circadian rhythms (CR) could have an adverse effect on the body during adaptation to weightlessness and postflight recovery. Indeed, adverse sequelae of CR changes (decline of efficiency, sleep impairment, a number of functional disorders) have been demonstrated on the exampi of transmeridian flights, as well as in crews of the Apollo spacecraft and Skylab orbital stations [10]. It was shown in experiments with primates that disruption of CR leads to impaired heat regulation [12].

What sort of CR changes can one expected during spaceflights? In mammals, CR are controlled by a system of endogenous, coordinated oscillators. Normally, these oscillators are stably synchronized (picked up) by external time-setters, primarily lighting conditions, and in turn they provide for synchronization in lower-lying branches of the CR system. Coordination of oscillators is implemented by neural and humoral routes [6, 18]. However, the change in circulation, internal secretion and neural impulsation, which develops in weightlessness, can attenuate or disrupt the link between rhythm-setting

hypothalamic centers and lighting conditions and/or rhythms that are being controlled. In this case, there can be effects similar to those observed with experimental disruption of function of suprachiasmic nuclei of the hypothalamus: phase shifts, separation of rhythms, their change to freely occurring states, arrhythmia [9]. Indeed, the possibility of mutual dyscoordination of CR of different animal functions has been convincingly demonstrated in experiments with monkeys [20]. Desynchronization of CR may also be a nonspecific response to a stress situation [1]. On the other hand, the dynamics of inflight physiological parameters should reflect, in addition to change in rhythms, changes in diverse elements of homeostasis, including the thermoregulation system, under the influence of hypogravity.

There are rather sparse data as yet concerning CR during spaceflights. The experiment with a Macaca nemestrina monkey aboard American biosatellite 3 [14], though it did reveal appreciable impairment of rhythmicity (appearance of free run of some rhythms with different periods), the reliability of the findings was questioned due to the generlaly poor condition of the animal, which expired soon after landing. In the USSR, there have been several studies of rat biorhythms aboard biosatellites of the Cosmos series. In an experiment aboard Cosmos-782, it was shown that CR of body temperature and motor activity of the animals exposed to weightlessness are maintained in a "captured" state [3], whereas aboard Cosmos-1129 it was shown that normal alteration of CR phases is possible after inverting lighting schedule [15, 17]. Yet, the fact that there was a decrease in expression of conidiation rhythms in the Neurospora fungus in an experiment aboard Spacelab-1 [22] is indicative of the possibility of CR disturbances in weightlessness. Extension of the free-running period and lag in CR phase of monkeys in altered gravity are of interest [13]. Thus, the question of probability, nature and type of CR changes during spaceflights remains open to this time, and this justifies continuation of research. We submit here the results of a joint Soviet-American experiment, "Biorhythm," aboard Cosmos-1514 biosatellite.

Methods

These studies were conducted on Macaca mulatta monkeys weighing 3-5 kg. Two monkeys, Abrek and Bion, were flown in space for 5 days. The conditions of ground-based control experiments differed only in that dynamic flight factors were lacking. As a control, we used 4 animals, one of which (Abrek) was examined in a biosatellite mockup 1 month before the flight. Before the experiment, the animals were kept in cages or primatological chairs. They were conditioned regularly to become accustomed to the regular immobilization system and feeding. An LD 16:8 lighting mode (ratio of light to dark periods) was established no later than 1 month before the experiment. During the experiment (both inflight and control), the animals were immobilized in BIOS capsules at LD 16:8 (lighting in the region of the animals head constituted 60±10 lux in daylight and 2±1 lux at night). Ambient temperature in the capsule was held at 23-25°C. The following daily schedule was established: 0000 to 0800 hours--nocturnal illumination, 0800 to 1000 h and 1600 to 1800 h—operator work with food reinforcement, 1000-1200 h and 1800-2000 h--mealtime.

In order to assess CR, we recorded body temperature (Tc), skin temperature (Ts) and motor activity (MA) of the animals. Tc in the axilla was measured via a

telemetry channel. The Tc sensor was implanted under the skin in the right axilla 2-3 weeks before the experiment. A plate Ts sensor (thermistor) was attached to a shaved area of the leg (lateral right malleolus) using cyacrin adhesive and secured with a thin mesh tape. A soft MA piezosensor was stitched on the vest that immobilized the monkey. Tc, Ts and MA values were recorded at 15-min intervals in a self-contained memory unit. The cumulative data obtained upon completion of the experiment were read and inputted in a computer. Mathematical data processing included periodogram analysis and calculation of averaged rhythm profile in a stationary segment of the curve.

Results and Discussion

Figure 1 (a, b) illustrates the general pattern of CR in the monkeys, Abrek and Bion during flight. Both animals retained marked Tc rhythms during flight, with maximum values (about 37.5°C) in the daytime and minimum (about 36.5°C) at night. Mean 24-h Tc gradually declined during the flight. There was a particularly noticeable decline of the nocturnal minimum. On the average, at each time of day Tc was reliably lower in Abrek during the flight than before it (Figure 2). The baseline data for Bion were not as representative; however, his mean Tc profile in flight was about the same as for Abrek: it is lower than the preflight profile for Abrek, and lower than the curve obtained for monkeys in the ground-based control. Thus, a decline of axillary Tc was observed in flight in both monkeys.

Preflight Ts ranged from 25 to 35°C. During the launch, both monkeys showed a brief elevation of Ts (see Figure 1). In weightlessness, Ts remained extremely low and exceeded ambient temperature by only 2-4°C. Abrek presented a rather regular rhythm, whereas Bion showed irregular (aperiodic) variations of Ts. It is only on the 5th flight day that the dynamics of Ts for Bion became the same as for Abrek. Thus, both monkeys showed a dramatic drop of leg temperature during the flight, and Bion also presented dissociation of Ts rhythm.

The circadian rhythms of MA remained distinct in both monkeys throughout the flight, with regular declines at night. Abrek was considerably more active than Bion: on the average, he performed 4 times more movements per unit time. Visual observation of the animals in flight, confirmed by videofilm, also revealed that Bion was not very active.

Periodogram analysis was performed (Figure 3) for more precise evaluation of CR periods. The amplitude of the circadian peak on the spectrum reflects the definition of rhythm: as can be seen in Figure 3, CR were more defined in Abrek than Bion. Unfortunately, because of the short duration of the experiment (less than 5 days), evaluation of the period was not very accurate: the apex of the daily peak, which was above the dotted line (corresponding to periods that were reliable at a level of $p<0.01$) was rather broad. Although the maximum on the Tc rhythm spectrum was other than 24 h (it occurred in the 25th h), this deviation could hardly be considered reliable. Thus, it should be concluded that Tc and MA circadian rhythms were locked in with the 24-h mode during the 5-day flight. However, the significance of this conclusion is limited in view of the inadequate duration of the flight experiment.

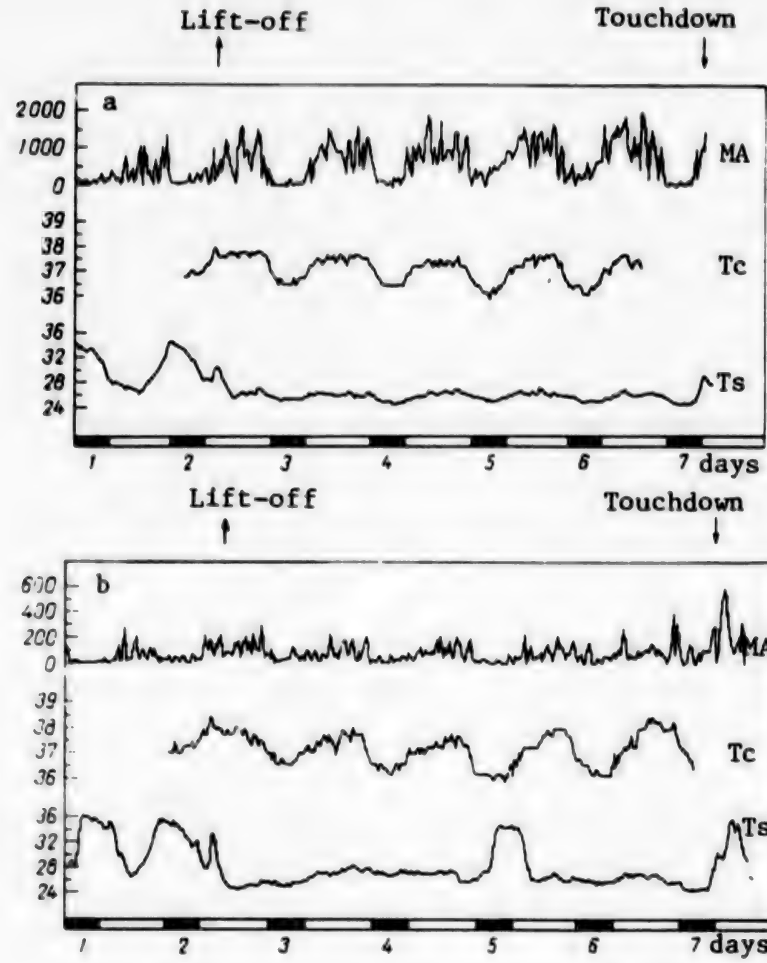

Figure 1. Circadian rhythms of MA, Tc and Ts in Abrek (a) and Bion (b)

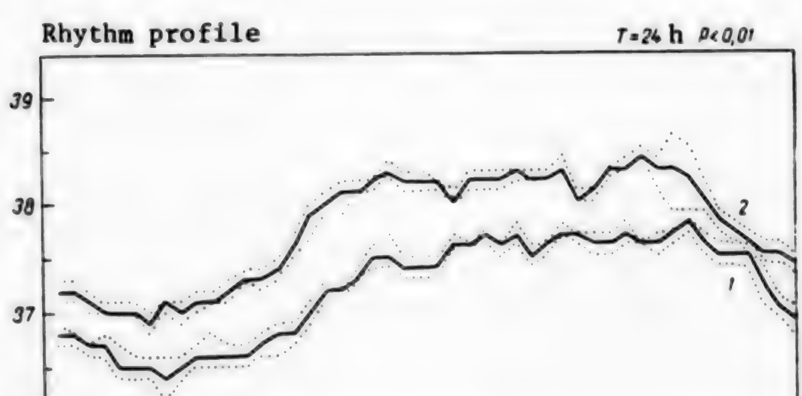

Figure 2. Averaged rhythm profile with standard deviations
1) Abrek during flight 2) Abrek in ground-based control experiment

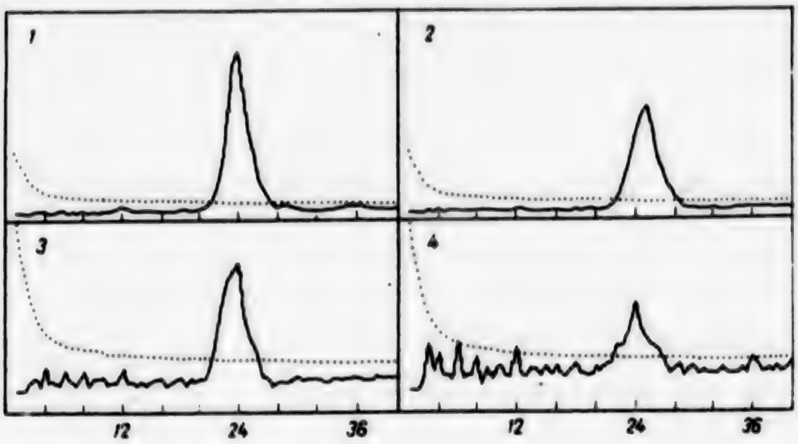

Figure 3. Periodogram analysis: inflight rhythm spectra of monkeys

1, 3) Tc and MA, respectively, for Abrek
2, 4) same for Bion

Dotted line shows confidence level, $p = 0.01$

The experiment conducted aboard Cosmos-1514 biosatellite confirmed that rather regular CR were retained and maintained during the flight. However, it should be borne in mind that throughout the experiment the animals were affected by a rigid light and dark regimen. Since it has been shown that primate CR are extremely sensitive to periodic changes in illumination [21] and are controlled by the feeding cycles [20], we are not clear about the extent to which the rhythms observed in flight reflect the activity of the actual circadian system and to what extent they are a reaction to the lighting conditions, as well as daily schedule of feeding and operator activity. In order to assess the function of the circadian system in weightlessness, it would be desirable to conduct a special experiment during a spaceflight: to examine the freely occurring CR under constant conditions (with "isolation from time").

To what extent is CR synchronized with the 24-h regimen in flight? Although the deviation from 24 h of the period of Tc rhythm in Bion was statistically unreliable, it is of some interest. It may be indicative of an early stage of development of desynchronization, or else, which is more likely, reflect the variability of the process (for example, change in rhythm profile or restructuring of rhythm phase as related to light cycles). Longer studies must be pursued to answer this question.

Some degree of hypothermia, which was observed in flight in both monkeys, was not unexpected. An analogous decline of mean 24-h body temperature occurred in rats used in an experiment aboard Cosmos-782 biosatellite [3]. Such an effect had also been demonstrated in man during dry immersion [2] and spaceflights [5], but not in head-down tilt position with hypokinesia [4]. There was gradual decline of Tc followed by a tendency toward recovery. What is the nature of this effect? Is it a passive reaction of the body when it is incapable of holding body temperature at the former level under new conditions, or is this an active, physiologically controlled reaction?

In rats, hypothermia in weightlessness could be attributable to two causes: in the first place, a shortage of heat production due to decrease in tonic

postural elements of muscle activity; in the second place, excessive heat loss at rest and during sleep, due to loss of postural control [2]. The latter factor could hardly have an important role for monkeys immobilized in chairs. As for muscular heat production, its contribution to overall heat production is rather considerable in these animals (weight 3-5 kg) according to indirect data [16]. Most of this heat is generated by slow muscles [11], which readjust in weightlessness and come closer in characteristics to rapid muscles [7]. Thus, a shortage of heat production in monkeys during a flight appears quite probable.

If this is so, then the reaction of maintaining temperature homeostasis should be manifested primarily by a decrease in blood flow and drop of Ts in the zones of physiologically controlled heat emission, i.e., in the distal parts of the extremities. Indeed, there was an inflight drop of Ts of the lower extremities of both monkeys, which could be either physiological compensation for cooling or the result of redistribution of blood volumes inherent in weightlessnes, in favor of the upper half of the body. The second assumption is more likely, since Ts dropped dramatically immediately after lift-off, whereas Tc dropped gradually. In such a case, the possibility of maintaining inflight body temperature should depend primarily on heat emission in the region of the animal's head which, in turn, depends on the cooling properties of the environment. But it is expressly in this area that ambient temperature was controlled by equipment that provided for thermal comfort. Thus, it should be noted that spaceflight conditions did not prevent maintenance of core Tc in monkeys.

Yet mean Tc did drop during the flight. It remains for us to assume that the Tc decline in flight did not evoke a controlling signal in the system of maintaining thermal homeostasis and was not associated with a compensatory response. In other words, the bottom of the range, within which Tc changes do not elicit a correction, shifted downward in weightlessness [8]. Apparently, removal of the static postural load was a factor that altered conditions of Tc regulation. According to [8], when the load on the system is diminished, the above-mentioned range is widened chiefly at the expense of decline of the bottom limit. For this reason, it should be expected that, at higher ambient temperature (and, in general, with less heat removal), Tc within this range may be even higher in flight than in the ground-based control. Thus, the hypothesis is that the body becomes, so to speak, "less homoiothermic" under the influence of weightlessness; Tc is controlled less precisely and depends more on the environment.

Thus, this experiment revealed some significant effects: decline of level and increase in amplitude of Tc rhythm, dramatic drop of Ts in monkeys during the spaceflight. It would be desirable to pursue further biorhythmological studies in space in order to identify the nature of these effects.

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EFFECT OF SPACEFLIGHT FACTORS ON PRIMATE HYDRATION HOMEOSTASIS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 17 Feb 87) pp 19-22

[Article by V. V. Zhidkov, S. V. Abrosimov, D. K. Endeka, G. I. Borisov, V. I. Lobachik, V. V. Korolkov and Ye. A. Ilyin]

[English abstract from source] Using nuclear physics methods, hydration homeostasis of three monkeys flown on Cosmos-1514 and Cosmos-1667 was investigated. Measurements were made before flight, 1.5 hours after touchdown and during the recovery period. Total water content, extracellular and tissue fluid volumes were measured and intracellular and interstitial fluid volumes were calculated. Postflight, all the animals showed hydration status changes of similar sign: total water content, intracellular and extracellular fluid volumes decreased. Most significant changes occurred in tissue and interstitial fluid volumes. Hydration status responses to space flight factors were variable and the above changes disappeared in the course of the recovery period. The variations recorded were viewed as adaptive.

[Text] The experience accumulated by cosmonautics has clearly defined the list of systems and functions of the body that are the most sensitive to spaceflight factors and, first of all, to weightlessness.

In this list, some of the changes in body fluids occupy a prominent place [1-3]. It is quite apparent that changes in hydration homeostasis have a direct and indirect effect on the condition and function of all systems, organs and tissues. In spite of the fact that some advances have been made by space physiology in the study of this direction, some important theoretical and applied questions remain little-studied.

To date, the mechanisms, routes and nature of formation of the hydration status have not been definitively identified; there is extremely sparse information about its infrastructure and the relationship between fluids and other body functions and systems both during flight and in the period of readaptation to earth's gravity. At the present time, there are some difficulties involved in conducting extensive and comprehensive studies of this highly dynamic function of man during spaceflights or immediately after their termination. Experiments with animals, which are conducted aboard Cosmos series biosatellites,

could make a significant contribution to the solution of a number of problems. We conducted studies of body fluid status in the monkeys, Vernyy and Gordyy, which were flown aboard Cosmos-1667.

Our objective was to examine the effect of factors involved in a 7-day spaceflight on primate hydration homeostasis.

Methods

Nuclear physics methods were used in this study. A quantitative assay was made of total body fluid volume (^3H_2O isotope, single dose 0.074 MBq) and of vascular fluid (^{131}I-albumin isotope, single dose 0.02 MBq). Extracellular fluid content was measured with use of stable bromine (single dose 0.05 g) followed by measurement of its concentration by the roentgenofluorescent method. Intracellular and interstitial fluid volumes were determined by the traditional mathematical method [4]; composition of the body was determined according to total dose in it [4-6]. The primates were examined in the baseline period, at the touchdown site and in the 4th month of the recovery period.

Results and Discussion

The results of the baseline examination of flight animals revealed that hydration homeostasis and its infrastructure were generally within the normal range of values inherent in healthy animals of the same age and weight. However, it should be noted that fluid fraction values for Vernyy and Gordyy before the flight were below the mean-group levels of back-up monkeys. The biosatellite capsule touchdown in a strictly specified region made it possible to rapidly deploy a field version of a radioisotope laboratory and begin the tests 1.5 h after landing.

Weighing the animals after the flight revealed that Vernyy lost 10 g, as compared to the baseline. The other monkey lost 140 g. Analysis of body composition of Vernyy revealed that the change in weight was referable primarily to lean body mass, which decreased by 17 g during the flight, or by 1% of the baseline. In Gordyy, lean body mass decreased during the flight by 42 g, i.e., by 2% of the baseline value, in the presence of increased fat body mass. Because of these distinctions, when analyzing fluids we considered both their absolute levels, which are indicative of the direction and extent of change, and their correlation with weight, which reflects hydration homeostasis.

As shown by the results of postflight examination, total water content diminished insignificantly in Vernyy, both in absolute and relative terms, constituting 97.7 and 97.9%, respectively, of baseline values (Table 1). In this monkey, intracellular fluid volume remained virtually the same as in the preflight period. Fluid level in the second monkey was found to be lower after the flight than before it, by 1.3% in absolute terms and by 4.8% when scaled to the altered body weight. The volume of the intracellular fluid space decreased by about the same value in this monkey. The 7-day spaceflight elicited a decrease in extracellular fluid in both monkeys, in both absolute and relative terms. In Vernyy, its volume constituted 95.3 and 95.7% in absolute and relative terms, respectively, of the baseline after touchdown. There were similar changes in extracellular fluid space in Gordyy.

Table 1. Status of body fluids of Gordyy and Vernyy before and after spaceflight

Parameter	Measurement unit	Vernyy			Gordnyy		
		pre-flight	post-flight	recovery period	pre-flight	post-flight	recovery period
TBW	mℓ	2262	2209	2510	2240	2210	2440
	mℓ/kg	560	548	564	541	515	542
EFV	mℓ	934	890	1004	915	905	987
	mℓ/kg	231	221	226	221	211	222
IFV	mℓ	1328	1320	1506	1325	1305	1443
	mℓ/kg	329	327	338	319	304	321
CPV	mℓ	192	174	190	205	191	202
	mℓ/kg	47	43	43	49	44	45
IsFV	mℓ	767	716	814	710	714	785
	mℓ/kg	190	178	183	171	166	177

Key for Tables 1 and 2:
TBW) total body water
EFC) extracellular fluid volume
IFV) intracellular fluid volume
CPV) circulating plasma volume
IsFV) interstitial fluid volume

Table 2. Correlation (%) between body liquid fractions of monkeys before and after 7-day spaceflight

Monkey	Testing time	IFV/TBW	EFV/TBW	EFV/IFV	IsFV/TBW	CPV/EFV	CPV/IsFV
Vernyy	Preflight (baseline)	58,7	41,3	70,3	82,1	20,5	25,0
	Postflight	59,8	40,3	67,4	80,4	19,5	24,3
	Recovery period	60,0	40,0	66,6	81,1	18,9	23,3
Gordyy	Preflight (baseline)	59,0	40,9	69,1	77,5	22,4	28,8
	Postflight	59,0	40,9	69,2	78,8	21,1	26,7
	Recovery period	59,2	40,4	68,3	79,6	21,1	25,7

Analysis of the infrastructure of the extracellular sector revealed changes in both animals in amounts of both vascular and interstitial fractions. We demonstrated a 6.3 and 2.9% decline in interstitial fluid when scaled to body weight. More marked changes after the flight were found in the vascular fraction. Absolute plasma volume was 9.4 and 6.8% lower in Vernyy and Gordyy, respectively.

It may be of some interest to analyze the distribution of body fluids and the correlations between them in flight monkeys at the indicated test times. A comparison of the data obtained preflight and un the 4th month of the recovery period can be generally characterized by the direction of formation of the hydration status in developing animals. Five-month follow-up on the animals revealed some changes in hydration homeostasis (Table 2). There was

a tendency toward increase in volume of intracellular fluid space, while fluid content in the extracellular sector had a tendency toward decline. There was also redistribution of fluid within the extracellular fluid space. Throughout the indicated period, we observed a tendency toward increase in specific gravity of interstitial fraction in the presence of decline in vascular fluid volume. Such redistribution of body fluid in young, developing animals changed in the direction of increase in specific gravity of intracellular and interstitial fluids, which was probably attributable to the need to assure adequate plastic function and metabolic activity in the developing organism.

Analysis of correlation between animal body fluids postflight revealed that the changes in hydration homeostatis caused by the 7-day spaceflight in Vernyy did not alter the correlation between fluid fractions. In Gordyy, we observed some tendency toward change in correlation between intracellular and extracellular sectors in favor of the latter, which is probably related to the more marked loss of lean body mass inflight, as compared to the first monkey. Fluid distribution in the vascular and interstitial fractions of Gordyy showed virtually no postflight change. In the 4th month of the recovery period, both monkeys showed an increase in all body fluids up to or above the baseline values.

Thus, there were changes in hydration homeostasis in both monkeys under the effect of the 7-day flight, which affected all elements of its infrastructure. However, it should be noted that the change in the function in question was less significant during the 7-day flight than the changes in hydration status of Abrek following a 5-day flight aboard Cosmos-1514. In this monkey, hydration of the body dropped to 95% of the baseline during the spaceflight. Volumes of intracellular fluid and extracellular water space diminished to 95.2 and 88.2%, respectively. Interstitial and vascular fractions were 7.5-19% lower after landing than in the baseline period. This animal lost more than 300 g after the 5-day flight, lean body mass diminished by 6.5%. All of the above changes reverted to their baseline levels after 30 days of the recovery period.

As can be seen from the submitted data, spaceflight factors caused similarly directed changes in hydration homeostasis in all three monkeys; they were manifested by decline of body hydration level and of amounts of virtually all body fluids. It should be noted that the most significant changes were recorded in extracellular fluid content, which is the most reactive fluid fraction of the body. Changes in this fluid occurred at the expense of both interstitial fluid space and vascular fluid. In actuality, all three monkeys showed changes in amount of intracellular fluid, which were almost entirely correlated with decrease in lean body mass.

This aspect of the changes is apparently indicative of diminished metabolic activity during the flight. However, in spite of the fact that the flights were brief, we cannot rule out appearance of atrophic changes in tissues of primarily the muscular system. It is deemed important to note that the quantitative changes in body fluids of the animals after the flight did not exceed the "norm" for healthy animals. In other words, hydration homeostasis was formed at a lower quantitative level consistent with the altered living conditions. The changes were adequate, functional in nature.

The obtained data reflect, to some extent, the hydration status at the last stage of the flight. Since the monkeys were not given any fluids after

landing and up to the time they were tested, the hydration level could hardly have changed appreciably in the landing period. It also seems unlikely that there could have been appreciable redistribution of fluid in the intracellular and extracellular space during the period of the spacecraft's descent from orbit. As for redistribution of fluid within the extracellular space after touchdown, it is quite likely. However, in view of the small number of cases, it is not possible to determine their direction and extent at this time.

It is quite apparent that investigation of animal hydration homeostasis may be quite beneficial and productive, in both the theoretical and practical aspects, with respect to answering a number of questions pertaining to the problem under discussion.

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EMBRYONIC DEVELOPMENT OF GUPPY IN WEIGHTLESSNESS

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[Article by Ye. M. Cherdantseva]

[English abstract from source] The program of the Cosmos-1514 flight included an experiment the purpose of which was to study the effect of weightlessness on the embryonic development of the live-bearing guppy fish: three pregnant females were flown for 5 days. Prelaunch their embryos were at the stage of cerebral vesicle differentiation and somite formation; this implies that the basic stages of organogenesis developed in weightlessness. One female was fixed in Bouin's fluid two days postflight and the second fish was fixed nine days postflight. Fourteen days after flight the third female gave birth to 25 normal fry. Thereafter that fish was mated 6 times more, each time delivering normal offspring. In addition, the offspring of the second generation was normal. Histological analysis of the embryos that were developing in weightlessness revealed no abnormalities. It can be concluded that weightlessness produced no effect on the fish development, begining with the stage of the axial complex formation.

[Text] Numerous experiments involving overturning and centrifuing emphibian eggs indicate that a change in direction of gravity elicits inversion of both animal-vegetative and dorsoventral polarity of the egg [5, 7]. At the same time, flight experiments (10] and experiments involving clinostating of developing eggs [1, 6] have shown that egg polarization can occur in weightlessness with compensation for earth's gravity as well. This means that gravity is not a mandatory factor in egg polarization, i.e., early morphogenesis is adapted to gravity just as it is to variable environmental factors. For this reason, in spite of the fact that gravity affects distribution of egg cytoplasm elements, there must be self-regulating mechanisms of polarization [2, 9], which are not only independent of gravity, but resistant to its change.

Methods

We used pregnant female specimens of the viviparous aquarium fish, the guppy, in our experiment.

The experimental aquarium with three pregnant guppies was flown aboard Cosmos-1514 biosatellite for 5 days. There were also three females in a control (on the ground) aquarium and synchronous experiment in a mock-up of the biosatellite. Temperature and upkeep conditions of control fish were the same as for the flight experiment. Two days after the biosatellite returned to earth, 1 gravid female from the experimental aquarium and 1 from the control aquarium were fixed in Bouin's fluid for subsequent histological analysis. The first fixing corresponded to about the 12th gestation day and the second (1 female from the experimental and 1 from the control aquarium) to 6 days later. One female was left in each aquarium to the time of spontaneous delivery.

Bouin's fluid was removed from the fixed females, the abdominal section containing the ovary was separate, stained with total boric carmine, desiccated and imbedded in paraplastic or epon. The obtained paraplastic serial sections, 6 μm in thickness, and semithin epon sections were additionally stained with solid green and analyzed under a microscope.

To determine egg orientation in the ovary at different developmental stages, females were fixed in Bouin fluid at different stages of pregnancy. Then the abdominal cavity of these females was opened, and the entire ovary was analyzed; in some cases it was additionally stained with methylene blue. In addition, we extracted and analyzed the ovary of unfixed gravid guppies, as well as the ovaries of adult unfertilized females.

Results and Discussion

The gravid guppies tolerated well the spaceflight conditions. Fixation of a control female on launch day revealed that in fish exposed to weightlessness the embryos were approximately at the stage of a formed axial complex and early differentiation of the brain. Thus, the basic elements of organogenesis occurred in weightlessness.

One of the experimental females left in the aquarium until delivery gave birth to 25 normally developed, actively swimming young fish and two abnormal, underdeveloped embryos. Such cases of birth of deformed embryos are also encountered when pregnant female guppies are kept under optimum conditions, and for this reason they could hardly be indicative of some specific effect of spaceflight factors on embryonic development. The gestation period in females flown in space constituted about 26 days, which is not beyond the range of individual variability of getation period under optimum upkeep conditions.

A control female gave birth to 20 normal fry on the 31st day of pregnancy. Considering the wide individual variability of female guppies with respect to fertility, it should be conceded that, according to this parameter also, no appreciable differences were found between the experiment and control. The results of the synchronous experiment did not differ from the control.

After parturition, a female from the experimental group was mated again with males to obtain a second generation of fry. In this female, the second gestation period lasted 26 days, i.e., just as long as the first pregnancy. This confirms, once more, that the difference between the experimental and

control females with respect to duration of gestation period is attributable to individuality of the females, rather than the effect of spaceflight factors. Since the second generation oocytes, starting at the stage of great growth, mature definitively only after birth of the first generation, oocyte maturation occurred already back on earth, so that the spaceflight conditions could have affected only the physiological condition of the females. Since the duration of the first and second pregnancies was about the same in the flight female, it can be assumed that spaceflight conditions did not affect either the physiological condition of females nor embryos at advanced stages of development.

Histological analysis also failed to demonstrate any differences between control and experimental embryos in the period from the stage of formed axial complex to the hatching stage.

In the course of the study, six generations of normally developed (to a puberal state) fry were obtained from experimental and control females. After this, in the seventh pregnancy, the females were fixed in Bouin fluid. Histological analysis revealed that the embryos were at the late-cleavage stage in experimental females, whereas in the control they were at the stage of completely formed axial complex and completely differentiated cerebral vesicles. In both instances, development was entirely normal.

Of the 25 fry developing during spaceflight for part of the embyronic period, upon reaching maturity 12 were found to be females and the rest males. These mature guppies were mated with one another, and they produced normal second-generation offspring.

Examination of egg orientation in the ovaries of control, unfertilized guppies revealed that mature unfertilized eggs are densely stacked in the ovary and do not have the proper spherical shape. After extraction from the ovary, within 30-60 min they acquired a more or less spherical form. Since the yolk sac adhered firmly to the egg surface in unfertilized eggs, egg orientation could be at random, in spite of the fact that, even unfertilized eggs showed animal-vegetative polarity manifested by the fact that there were accumulations of finer droplets of fat at one pole of the egg. In addition, this pole was virtually free of cytoplasm, which lay on the periphery of the remaining part of the egg. Due to the dense packing in the ovary, the eggs were rather severely deformed, and the direction of deformity was unrelated to the direction of animal-vegetative polarity; rather, it depended on the egg's position in the ovary.

After fertilization, the yolk sac separated from the egg's surface, and a small perivitelline space was formed. Nevertheless, during cleavage and at subsequent stages of development, the eggs remained densely packed in the ovary and just as deformed.

Live eggs extracted from the ovary and separated from one another acquired a spherical shape within 50 min; however, the orientation of their animal-vegetative axis in relation to the vertical plane was inconsistent. Histological analysis revealed that there are differences between the animal and vegetative parts of the yolk sac, which are manifested by the fact that

during cleavage there was concentration of lipid droplets under the blastoderm, i.e., in the animal part of the yolk sac.

During cleavage, the eggs were densely packed in the ovary and oriented primarily with the animal pole (i.e., blastoderm) up in relation to the maternal abdominal cavity. Other embryos were on their side, and a few of them were oriented with the animal pole down. Such distribution of orientation persisted until the fry was completely formed. Analysis of quantitative data indicates that about 37% of the fry were oriented with their head up, about 38% were lying on their side and about 25% were turned head down. The anterioposterior axis of embryo lying next to one another in the ovary showed either the same or different orientation. Thus, there was no standard orientation of developing eggs.

The eggs of the same generation were at similar stages of development in the ovary, although some of the eggs could be lagging in development from the majority. For example, we encountered eggs at the cleavage stage that were 2-3 divisions behind, or at the time when most (about 70%) embryos were at the stage of formed eyes and olfactory capsues, some were still at the stage of differentiation of cerebral vesicles.

Thus, analysis of normal development revealed that polarity of guppy eggs most probably is unrelated to the direction of gravity, as was assumed by some authors [4, 8]. Nevertheless, we believe that there is no contradiction between this fact and data pertaining to the relative role of rotation of fertilization in determining the direction of the dorsoventral axis [3]. According to our observations, an isolated egg could indeed revolve in the yolk sac, assuming equilibrated orientation in the gravity field. However, if we bear in mind that eggs are densely stacked in the ovary and are not spherical, apparently a fertilization turn is impossible for most eggs. Thus, a fertilization turn could play some part in determination of dorsoventral polarity, but not for all eggs, i.e., it is not a mandatory factor of polarization.

The biology of guppy development is such that adaptation to viviparity in itself should be instrumental in stable development and change in direction of the effect of gravity. In view of the small size of the ovary there is an obvious need for dense stacking, since the number of developing eggs is relatively large. Such dense packing inevitably leads to deformation of the eggs. Let us recall that a spherical shape is equilibrated for isolated eggs. As we have already stated, deformation of guppy eggs leads to redistribution of yolk in the egg, which is individual for each egg. This means that, in the course of its development, the egg is exposed to the effect of mechanical tension considerably greater than could be caused by normal gravity. Egg development is not directly dependent on the distinctions of yolk distribution in the yolk sac. Consequently, resistance to gravity should be an indirect result of developmental resistance to deformation leading to redistribution of yolk in the yolk sac.

Thus, the absence of effect of weightlessness, staring in the period of organogenesis, can be considered experimentally proven. On the other hand, according to the observations described above with respect to normal development of guppies, it can be concluded that weightlessness will not affect morphogenesis at the very earliest developmental stages as well.

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HISTOMORPHOMETRIC ANALYSIS OF RAT BONES AFTER SPACEFLIGHT ABOARD COSMOS-1667 BIOSATELLITE

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[Article by A. S. Kaplanskiy, G. N. Durnova, Z. F. Sakharova and Ye. I. Ilyina-Kakuyeva]

[English abstract from source] Bones of the rats flown on Cosmos-1667 were examined histologically and histomorphometrically. It was found that 7-day exposure to weightlessness led to osteoporosis in the spongy matter of proximal metaphyses of tibia and, although to a lesser extent, in the spongiosa of lumbar vertebrae whereas no signs of osteoporosis were seen in the spongy matter of iliac bones. Osteoporosis in the spongy matter of the above bones developed largely due to the inhibition of bone neoformation, which was indicated by a decrease in the number and activity of osteoblasts. Increased bone resorption (as shown by a greater number and activity of osteoclasts) was observed only in the spongy matter of tibial metaphyses. It is emphasized that a reduction of the number of hihgly active osteoblasts in spongy bones is one of the early signs of inhibition of bone neoformation and development of osteoporosis.

[Text] Previous studies of bones of rats blowin aboard biological earth satellites of the Cosmos series revealed that 18-22-day exposure to weightlessness leads to decline in bone strength [4-6, 8]. Development of this phenomenon is attributed to loss of mineral component of bones [1-3, 7, 20] and onset of osteoporosis [3, 7, 10-12, 16, 23]. Inhibition of de novo osteogenesis is undoubtedly one of the causes of osteoporosis that develops in weightlessness [9, 16-23], and it is due to decrease in number and functional activity of osteoblasts [14, 16, 18-20]. Thus far, the question of whether this is associated with intensification of bone resorption is open: some authors deny this [13, 16, 20], while others adhere to the opposite view [1, 7, 10, 11].

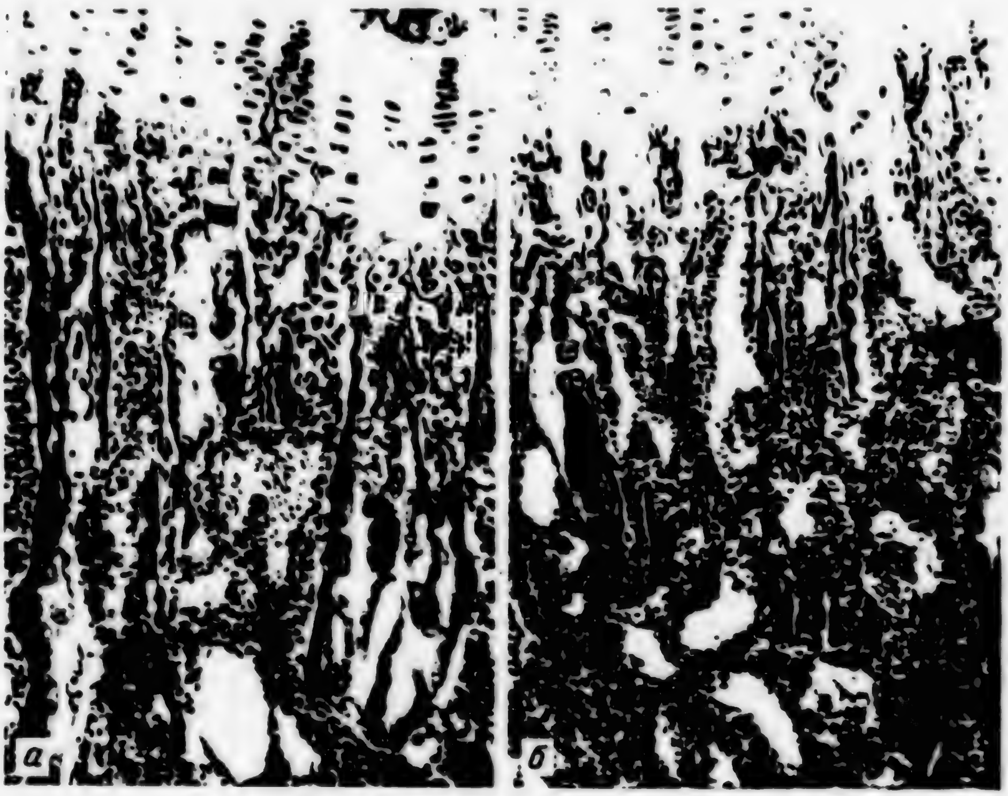
We submit here the results of examining bones of rats exposed to weightlessness for 7 days. We needed to answer the following questions: 1) Does relatively brief exposure to weightlessness cause development of osteoporosis in animals and what are its early morphological signs? 2) How do bones that carry

different functional loads react to brief weightlessness? 3) to what is development of osteoporosis in rats in weightlessness related—only inhibition of de novo osteogenesis, or with additional intensification of bone resorption? To answer the last question, we deemed it expedient to devote special attention to examination of osteoblasts and osteoclasts, since the rate of de novo osteogenesis and bone resorption ultimately depends on the functional state of cells.

Methods

The tibia and iliac bones, as well as lumbar vertebrae of 28 male Wistar rats weighing 300-350 g served as the material for our study. The animals were divided into four SPF [free of specific pathogenic microorganisms]. equal groups (7 rats in each): the 1st group consisted of lats flown aboard Cosmos-1667 for 7 days and sacrificed 4-8 h after its landing; the 2d group—vivarium control animals; 3d group—rats used in a ground-based synchronous experiment, in which physiologically significant spaceflight factors were simulated (with the exception of weightlessness), and the 4th group consisted of vivarium controls for rats in the ground-based synchronous experiment. After weighing the animals, all were decapitated. Muscles were removed from the bones, and they were fixed in 4% neutral formalin prepared in 10% EDTA solution. After 2 days, the bones were transferred into 10% EDTA solution for decalcification, which lasted 14 days. The bones were then washed in tap water; the proximal third of the tibia was separated, and a 2 mm tall segment was excised from the diaphysis at the level of its attachment to the fibula. All of the bones were dehydrated in alcohol and imbedded in "Histoplast." Longitudinal serial sections of the proximal end of the tibia and lumbar vertebrae, which were cut parallel to the frontal plane, transverse sections of the tibial diaphyses and sections of iliac bones 5 μm in thickness were cleared of paraffin and stained with hematoxylin and eosin, picrofuchsin, tuluidine blue, methyl green-pyronine and by the Schmorl method. An MOV-15 ocular micrometer was used to measure the thickness of the cartilate growth plate and length of primary spongiosa trabeculae on sections of the proximal ends of tibia, vertebrae and iliac bones. Volume density of primary and secondary spongiosa was measured by the dot method, using the morphometric grid of S. B. Stefanov. The latter was also used to count the haversian canals in compact bone of tibial diaphyses. The external and internal perimeters of tibial diaphyses, area of cortical plate of diaphyses and medullary cavity, as well as area of haversian canals and osteocytic lacunae were determined using an image analyzer. Osteoblasts in the spongiosa of lumbar vertebrae, iliac bones and metaphyses of tibial bones were counted in 25 microscope fields at 900× magnification. In addition to the total number of osteoblasts, we calculated the percentage of highly, moderately and minimally active forms, for which purpose we counted 500 cells. Large polygonal cells with eccentric nucleus and extensive pyroninophilic cytoplasm containing a large clear "cavity" in the perinuclear zone and low nucleus/cytoplasm ratio were classified as highly active. The moderately active osteoblasts were polygonal or elongated cells of considerably smaller size than the highly active ones, with pyroninophilic cytoplasm containing no "cavity," with eccentric nucleus and a nucleus/cytoplasm ratio of 1/1-1/2. Elongated, fusiform cells with insignificant pyroninophilic cytoplasm, eccentric nucleus and high nuclus/cytoplasm ratio were considered as having low activity. Total osteoclasts in the primary spongiosa zone of vertebrae

and iliac bones was determined. In the proximal metaphyses of tibial bones, osteoclasts were counted separately underneath the growth plate and in the zone of remodeling of primary spongiosa into secondary. In addition to total number of osteoclasts, we determined the number of active ones, referring to cells spread out on the surface of bone trabeculae or in resorption lacunae. Osteoclasts were counted in 20-25 microscope fields at 900× magnification. The obtained digital data were submitted to statistical processing according to Student, considering differences reliable at $p<0.05$.



Osteoporosis in rat tibia after 7-day flight aboard Cosmos-1667

a) spongiosa of proximal metaphysis of control rat tibia
b) spongiosa of proximal metaphysis of rat tibia after 7 days aboard Cosmos-1667

Picrofuchsin stain, magnification 63×

Results and Discussion

The results of histological and histomorphometric examination of tibial bones indicate that, in spite of the relatively shoft duration of the spaceflight, there were distinct signs of osteoporosis. Presence of the latter was confirmed by both visual examination of histological preparations (see Figure, a and b) and on the basis of decline of volume density of primary and secondary spongiosa, as well as decrease in length of trabeculae of primary spongiosa (Table 1). Volume density of primary and secondary spongiosa, as well as length of primary spongiosa trabeculae, decreased by 12.36 and 29%,

respectively, as compared to the control. There was no change in thickness of the cartilaginous growth plate of the epiphysis. Absence of changes in thickness of the growth plate in the presence of osteoporosis had been noted previously after analysis of rat tibial bones after 18.5-day flight aboard Cosmos-782 [10].

Table 1. Results of histomorphometric analysis of tibial metaphyses

Parameter studied	Animal group			
	1	2	3	4
Growth plate thickness, μm	210±6,0	210±6,0	190±5,0	190±5,0
Length of primary spongiosa trabeculae, μm	320±8,0*	460±8,0	360±7,0*	430±12,0
Volume density of primary spongiosa, %	44,3±1,1*	50,4±0,4	44,9±2,0	47,3±0,7
Volume density of secondary spongiosa, %	18,5±0,9*	28,8±0,5	23,9±1,0*	29,0±1,7
Osteoblasts:				
per visual field	23,4±1,8*	28,3±1,2	19,2±0,6*	21,6±0,8
highly active, %	17,7±1,3*	29,7±1,9	16,7±1,5*	21,0±1,4
moderately active, %	70,3±1,9*	63,2±2,6	76,4±0,8	75,2±1,3
minimally active, %	11,9±2,0*	6,1±1,0	6,9±0,9	3,6±0,6
Osteoclasts underneath growth plate:				
number per field	1,8±0,2	1,5±0,2	2,1±0,2	2,4±0,3
Osteoclasts in remodeling zone:				
total number per field	2,3±0,1*	1,8±0,2	2,0±0,1	2,2±0,2
number of active cells per field	1,7±0,2*	1,2±0,1	1,4±0,1	1,4±0,1

*Here and in Tables 3 and 4: statistically reliable differences between experiment and control.

Concurrently with development of osteoporsis in spongiosa of tibial metaphyses, there was 18% decrease in number of osteoblasts. There was decrease not only in total number of cells, but percentage of highly active forms of osteoblasts, with concurrent increase in number of moderately and minimally active forms (see Table 1). A decline in functional activity of rat osteoblasts had also been demonstrated following a 7-day flight aboard Spacelab-3 with exposure of rats to weightlessness [15]. In addition, in the osteoblast population there was appearance of cells with signs of dystrophic damage (vacuolization of cytoplasm, vagueness and irregularity of cell outline, decreased pyroninophilia of cytoplasm).

Analysis of the osteoclast population revealed that the number of these cells right under the growth plate increased somewhat; however, this increase was statistically unrelaible, whereas the increase in number of osteoclasts in the region of remodeling reached a statistically significant value (see Table 1). There was also increase in number of active osteoclasts. According to the data listed in Table 2, no changes, as compared to control animals, were demonstrable in tibial diaphyses of the flight group of rats.

In the ground-based synchronous experiment animals, osteoporosis of spongiosa of the tibial metaphyses was considerably less marked. Although the total

number of osteoblasts and highly active osteoblasts did diminish, the decline was less marked than in the flight group of rats (see Table 1). No changes were observed in the osteoclast population. The tibial diaphyses did not differ from those of the vivarium control group with regard to parameters studied (see Table 2).

Table 2. Results of histomorphometric analysis of tibial diaphyses

Parameter studied	Animal group			
	1	2	3	4
Outside perimeter of diaphysis, mm	12,3±0,3	12,0±0,1	12,8±0,4	12,7±0,6
Inside perimeter of diaphysis, mm	6,0±0,3	5,8±0,1	5,9±0,2	6,2±0,7
Cortical plate area, mm^2	8,6±0,4	8,4±0,4	9,5±0,8	9,8±0,7
Medullary cavity area, mm^2	0,9±0,07	0,9±0,04	0,8±0,04	0,9±0,1
Haversian canals (per 20 squares of Stefanov grid)	87,4±4,1	93,8±1,8	89,3±4,3	92,6±3,3
Haversian canal area, μm^2	136,3±18,7	161,7±13,9	167,3±7,6	176,8±13,6
Single osteocyte lacuna area, μm^2	43,8±5,0	40,3±1,3	47,6±2,7	53,4±2,4

Table 3. Results of histomorphometric analysis of lumbar vertebrae

Parameter studied	Animal group			
	1	2	3	4
Growth plate thickness, µm	145±3,5*	132±4,5	132±1,7	132±2,9
Primary spongiosa trabecular length, µm	178±7,7	185±7,4	166±7,0	173±8,0
Primary spongiosa volume density,%	58,2±1,3*	66,4±1,5	60,8±1,4	62,8±1,1
Secondary spongiosa " " "	30,6±1,3*	34,7±1,1	34,0±2,4	30,8±1,4
Osteoblasts:				
per visual vield	15,1±0,8	16,2±1,1	14,1±1,2	12,9±1,3
highly active, %	7,7±0,9	11,4±2,4	7,1±1,2	6,5±1,0
moderately active, %	75,4±1,8	79,1±2,7	73,4±2,0	72,3±3,7
minimally active, %	16,9±0,9*	9,7±2,3	19,4±0,8	21,2±3,9
Osteoclasts in zone of primary spongiosa: number per field	2,0±0,1**	2,3±0,1	2,2±0,1	2,2±0,2

**Here and in Table 4: borderline reliability of differences between experiment and control (0.05<p<0.1)

In addition to the spongiosa of tibial metaphyses, early signs of osteoporosis were demonstrable as well in the spongiosa of lumbar vertebrae in the flight group of rats. However, it was considerably less marked in vertebrae than in the tibia. Thus, volume density of vertebral secondary spongiosa diminished by only 12%, whereas in the tibial bones it diminished by 36%; the length of primary spongiosa trabeculae in the vertebrae was virtually the same as in the control, whereas in the tibial bones it diminished by 29%. There was no change in number of osteoblasts in lumbar vertebrae of flight group rats, but the percentage of highly active forms decreased, with concurrnet increase in inactive cells (Table 3). As for osteoclasts, the vertebrae of these rats

showed a distinct tendency toward decline in their number, which is apparently the cause of increased thickness of vertebral cartilaginous growth plate (see Table 3). Thus, while exposure of flight group of rats to weightlessness led to increase in number and activity of osteoclasts in their tibial bones, the opposite tendency was observed in the vertebrae. As shown by our studies, the causes of this phenomenon are not clear, and we can merely mention that, when simulating weightlessness (by "suspending" the rats in antiorthostatic [head down tilt] position) there was some decrease in number of vertebral osteoclasts, whereas their number increased reliably in tibial metaphyses. No changes were demonstrable in the vertebrae of rats used in the ground-based control experiment, as compared to their vivarium control.

Table 4. Results of histomorphometric analysis of iliac bones

Parameter studied	Animal group			
	1	2	3	4
Growth plate thickness, μm	171±5	174±2	160±7	170±5
Primary spongiosa trabecular length, μm	200±11	222±13	130±3	144±7
Primary spongiosa volume density,%	42,8±2,4	45,6±1,4	35,2±1,7*	40,0±0,8
Secondary spongiosa " " "	14,8±1,2	17,2±1,2	18,0±1,6	18,4±1,2
Osteoblasts:				
per field	20,2±3,0**	27,0±1,6	14,4±0,8*	18,6±1,1
highly active, %	14,5±2,7**	21,0±2,0	6,9±1,2**	10,5±1,3
moderately active, %	75,0±1,6**	69,2±2,3	73,1±1,7*	81,5±1,3
minimally active, %	10,5±1,1	9,4±0,8	20,0±1,5*	8,1±1,6
Osteoclasts in primary spongiosa zone:				
number per field	2,9±0,2	3,1±0,1	3,4±0,4	3,7±0,1

After exposure of rats to weightlessness for 7 days, volume density of primary and secondary spongiosa of the iliac bones, as well as length of trabeculae of the primary spongiosa were somewhat lower than in the control, although the differences did not attain statistically reliable values. At the same time total number of osteoblasts and percentage of highly active osteoblasts diminished in the iliac spongiosa, while the number of osteoclasts did not change (Table 4). Analogous findings were made upon histomorphometric analysis of iliac bones of rats used in the ground-based synchronous experiment (Table 4).

To sum up the foregoing, it should be considered that osteoporosis starts to develop in rat bones at the acute phase of animal adaptation to weightlessness, and at this stage distinct signs of osteoporosis are demonstrable in the spongiosa of tibial metaphyses. Although there is osteoporosis of vertebral spongiosis, it is considerably less marked, while no signs of osteoporosis are evident in the iliac spongiosa at this time. These differences in reactions of different bones to the same factor are most probably related to differences in metabolism and functional loads experienced by the bones, maximum changes being observed in intensively growing bones with high metabolism that carry a large load. It should also be emphasized that, while inhibition of de novo osteogenesis (as indicated by the decrease in number and functional activity of osteoblasts) was noted in all bones examined, signs of intensification of

osteoclastic bone resorption were demonstrated only in the tibial metaphyses. The question of whether the intensification of bone resorption is specific to weightlessness for the tibial bones, or whether this process is also inherent in other bones, but occurs after longer exposure to weightlessness, remains open. Differential counts of osteoblasts enabled us to establish that decrease in number of highly active osteoblasts and appearance among them of cells with dystrophic damage are the earliest, although indirect, signs of incipient osteoporosis. This is not associated with change in total number of osteoclasts.

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UDC: 612.35.014.2:612.6.05:577.213.7].014.477-064

EFFECT OF WEIGHTLESSNESS ON REPLICATIVE FUNCTION OF RAT HEPATOCYTE DNA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 5 Sep 86) pp 31-34

[Article by G. S. Komolova, A. V. Zakaznov and V. F. Makeyeva]

[English abstract from source] The replicative function of DNA of liver cells of rats exposed to strong stress effects, e.g. suspension for 2.5 hours a day for 6 days, decreased. The rat studies onboard biosatellites of the Cosmos series have demonstrated that a prolonged exposure to microgravity (up to 22 days) is not a stressogenic factor for the DNA synthetic system of liver cells. The transition from 1 g to microgravity cannot be viewed as a strong stressor either, because the rate of DNA synthesis in liver cells at an early period of adaptation to microgravity remains within the normal limits. However, this parameter decreases significantly during the recovery period following 18-22-day flights. Therefore changes in cellular processes related to the DNA replicating function in hepatocytes should be expected to occur in the postflight period rather than at an early period of adaptation to microgravity.

[Text] There is still insufficient information about the nature and severity of stress responses of the genetic system of animal cells to spaceflight factors. This also applies to the DNA-synthesizing system, which is functionally related to such vital cellular processes as proliferation and repair.

Our objective here was to make a comparative analysis of the effect of a gravity gradient on replicative function of rat hepatocyte DNA, which occurs at the first stage of spaceflight, when changing from earth's gravity to weightlessness and returning to earth.

Methods

In flight experiments, male Wistar rats were flown aboard spacecraft of the Cosmos series. The conditions of this series of experiments are described elsewhere [7, 8]. For all flight experiments, with the exception of the vivarium control, there was a ground-based synchronous control, in which all of the relevant physiologically significant spaceflight factors (with the

exception of weightlessness) were simulated. This enabled us to single out the effects of microgravity.

In model experiments with hypokinesia, the animals were kept in special box-cages that restricted mobility severely. Control animals were on the same food and drink regimen, but kept in the usual vivarium cages, 20×20×33 cm in size, with 5 animals in each.

As an additional stress factor, the animals were submitted to immobilization, in the form of stretching for 2.5 h/day for 6 days. We assessed replicative function of liver cell DNA according to incorporation of labeled precursors, in vivo and in vitro, using methods described previously [2, 6]. In all instances, we counted specific radioactivity, which was expressed in counts per migrogram DNA per minute, or percentage of vivarium control taken as 100. We analyzed 7-10 animals in each experimental variant for the parameters under study.

Results and Discussion

Long-term exposure to weightlessness, as well as abrupt change from weightlessness to earth's gravity, do not elicit changes in DNA-synthesizing activity of rat hepatocyte nuclei. As can be seen in Figure 1, the intensity of uptake of labeled precursor in nuclear DNA on the 1st day after 18-22-day flights did not differ appreicably from the vivarium and synchronous controls.

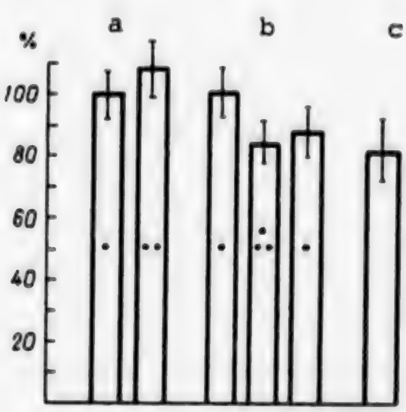

Figure 1.
Intensity of incorporation of radioactive precursor in nuclear DNA of rat hepatocytes following spaceflights lasting 19.5 days (Cosmos-782), 18.5 days (Cosmos-1129) and 22-day hypokinesia. Y-axis, specific radioactivity of DNA
a) Cosmos-782 c) hypokinesia
b) Cosmos-1129
*Vivarium control
**Flight
***Synchronous control

In the model experiments with 22-day hypokinesia, there was only a slight tendency toward decrease in synthesis of hepatocyte nuclear DNA. Since hypokinesia is an adequate model of weightlessness, it can be assumed that the response of the system in question to such stressors as insufficient motor activity or inadequate load on the locomotor system during long-term exposure to weightlessness is not significant.

At the same time, there was depression of replicative function of hepatocyte DNA a few days or even a week after returning to earth. Thus, on the 6th day after the flight aboard Cosmos-1129, there was 31% decline in DNA synthesis in hepatic nuclei, as compared to the vivarium control. This decline was also reliable in comparison to the synchronous control. Depressed synthesis of DNA in the liver was also demonstrable at later postflight stages. After the spaceflight aboard Cosmos-782, there

was 39% decrease in uptake of radioactive thymidine in nuclear DNA, as compared to the vivarium control. This indicates that the changes that occur in the DNA-synthesizing system are not transient; rather, they are protracted.

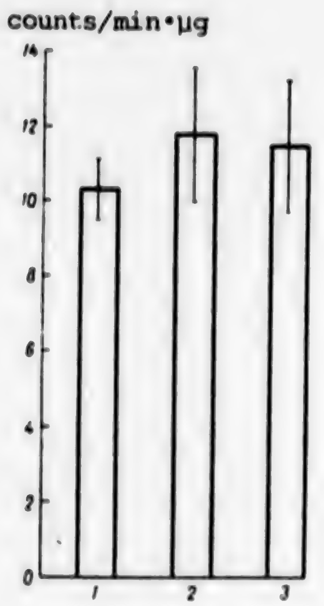

Figure 2.
Effect of 7-day flight aboard Cosmos-1667 on incorporation of radioactive precursor in nuclear DNA of rat hepatocytes.
Y-axis--specific radioactivity (counts/µg/min)
1) vivarium control
2) synchronous control
3) flight

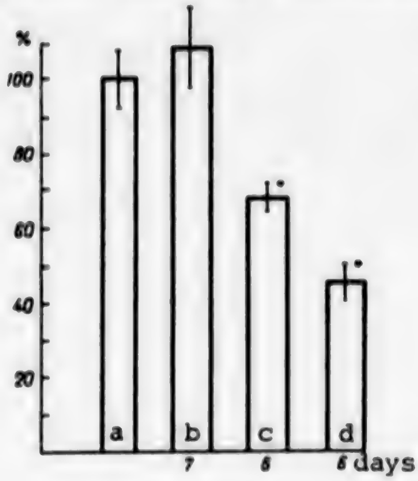

Figure 3.
Effect of gravity stress on incorporation of radioactive precursor in nuclear DNA of rat hepatocytes
X-axis--time of exposure (days);
y-axis--specific radioactivity of DNA (%)
a) vivarium control
b) earth's gravity → weightlessness (Cosmos-1667)
c) weightlessness → earth's gravity (Cosmos-1129)
d) immobilization
*Reliable differences as compared to vivarium control.

The above-mentioned changes in the genetic system of hepatocytes should probably be referred to stress responses of the chronic type. This is indicated, in particular, by the absence of additivity of effects of recovery and additional immobilization stress [6]. Immobilization of the animals, in the form of stretching for 6 days, at the rate of 2.5 h daily, elicited a decline in replicative function of hepatocytes which is typical of severe chronic stress. In the case of immobilizing animals in the flight group, the effect of this additional factor in the presence of the readaptation response was not evident. This may be indicative of adequate mechanisms, upon which both stress responses are based. There is reason to assume that the observed depression of replicative function of hepatocyte DNA is attributable to a change in growth hormone level. Indeed, in the postflight period, the change from weightlessness to earth's gravity is associated with decline of this hormone in the pituitary and plasma [1]. It is known, that there is no appreciable change in secretion of hormones of the adrenal medulla and cortex in the recovery period [3, 4]. Depression of mitotic activity and DNA synthesis by hepatocytes occurs only when

large, nonphysiological doses of glucocorticoid are administered. However, the tested parameters are quite sensitive to secretion of growth hormone [5].

Replicative function of rat hepatocyte DNA was tested in an experiment conducted aboard Cosmos-1667, after a brief (7-day) spaceflight. The data illustrated in Figure 2 indicate that intensity of incorporation of labeled precursor (^{3}H-TTP) in DNA of hepatic nuclei of rats in the flight group did not differ reliably from either the vivarium or synchronous control. Consequently, 7-day weightlessness, like that of longer duration (up to 22 days), does not affect the DNA-synthesizing system of liver cells.

Thus, the system studied is sensitive to transition from prolonged weightlessness to earth's gravity, but does not react to a gravity gradient occurring at the early stage of flight, due to disappearance of gravity. Figure 3 graphically demonstrates this difference. Considering the fact that animals exposed to "-" and "+" gravity gradients were sacrificed at similar times, it is possible to compare the effects induced by these gradients.

Figure 3 illustrates also the effect on replicative function of rat hepatocytes of a relatively strong stressor, immobilization, in order to assess the severity of the stress response that occurs with gravity changes. DNA synthesis in liver nuclei showed virtually no change when changing from earth's gravity to weightlessness, but with the reverse change it diminished just as it did with immobilization.

On the basis of our findings, it can be concluded that appearance of changes in the animal liver, which are related to replicative function of DNA, should be expected more during the period of readaptation to earth's gravity than at the early stages of a spaceflight.

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RNA-SYNTHESIZING ACTIVITY IN RAT LIVER FOLLOWING FLIGHT ABOARD COSMOS-1667

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 15 Aug 86) pp 34-36

[Article by V. F. Makeyeva and G. S. Komolova]

[English abstract from source] The effect of a short-term flight (7 days) on the RNA synthetic activity in isolated nuclei of the rat liver and its content of nucleic acids was investigated. Postflight the activity of RNA-polymerase, the key enzyme of RNA synthesis, increased. The endogenous synthesis of RNA in nuclei grew, probably due to the change in the activity of RNA-polymerase. Conversely, the concentration of nucleci acids in the liver tended to decrease. The results obtained give evidence that the changes in the RNA synthetic apparatus of hepatocytes in short-term flights are similar in sign to those seen in long-term flights.

[Text] Reversible functional changes were demonstrated in nucleic acid metabolism of rats during long-term (up to 22 days) spaceflights [2, 5]. In particular, we have shown that there is activation of the RNA-synthesizing system of the liver of male rats [3]. The question of condition of the genetic system of animal cells in the case of a brief spaceflight had not been explored heretofore. We determined in this study the RNA-synthesizing activity of isolated rat liver nuclei, activity of solubilized RNA polymerase and levels of nucleic acids.

Methods

Two series of experiments were performed with male Wistar rats: 1) flight experiment, in which the animals were flown aboard Cosmos 1667 for 7 days, and 2) a synchronous experiment, in which the main spaceflight conditions were simulated on the ground in a mock-up of a biosatellite.

Since material was collected at different times in the flight and synchronous experiments, we used a separate vivarium control (intact animals) for each, on the day of collecting specimens. We shall submit here the mean data obtained from 3-4 readings on 7 animals immediately after the experiments.

Nuclei were isolated from hepatic tissue by the method in [9]; some were used to determine endogenous RNA synthesis, while the rest were used to isolate solubilized RNA polymerase [8]. We assessed RNA synthesis in nuclei and enzyme activity according to intensity of incorporation of radioactive precursor ^{3}H-UMP in the acid-fast product of the RNA polymerase reaction. The results were expressed in counts/μg DNA/min. The conditions for determining endogenous RNA synthesis in nuclei and activity of RNA polymerase were described in detail previously [6]. Radioactivity of specimens was measured using an SL-4000 liquid scintillation counter (made in France). Nucleic acid content was determined by spectrophotometry and expressed in mg/g wet tissue [7].

Results and Discussion

The table lists the results of measuring nucleic acid content in hepatic tissue. It was found that DNA concentration was somewhat lower (by 15%; p = 0.05) in the liver of the flight group of animals than in the vivarium control. There was also an insignificant decrease (7%; p>0.05) in RNA content. There were changes in an analogous direction in animals used in the synchronous experiment; however, the changes were somewhat more marked under these conditions, by 19% and 12% for DNA and RNA, respectively, than in the flight group. It can be assumed that the set of factors associated with spaceflight but wanting in the synchronous experiment (in particular, weightlessness), prevented, to some extent, the inflight development of these changes.

Nucleic acid content (mg/g) in rat liver following flight aboard Cosmos-1667 (M±m)

Experiment	DNA	%	RNA	%	RNA/DNA
Flight	3,05±0,18	85	12,9±0,65	93	4,2±0,67
Flight control	3,57±0,13	100	13,8±0,42	100	3,8±0,44
Synchronous	2,70±0,17	81	12,1±0,52	88	4,5±0,53
Control for synchronous exp.	3,34±0,20	100	13,7±0,48	100	4,1±0,53

A comparison of the data obtained to the results of studies pursued aboard Cosmos series biosatellites in flights lasting 18 and 22 days [2, 3], reveals that even in the latter cases there were slight changes in nucleic acid content. Since these differences from the control were not always statistically significant, we can refer merely to a tendency toward decrease in concentration of nucleic acids when animals are exposed to spaceflight factors.

The nucleic acid level in cells is determined largely by synthesis of these acids. It was interesting to examine RNA-synthesizing activity in hepatocyte nuclei. Figure 1 illustrates experimental data on endogenous RNA synthesis in siolated nuclei of the rat liver. According to the data in this figure, transcription activity increased by 30% after the spaceflight, as compared to the same parameter for the vivarium control. Hepatic nuclei of animals used in the synchronous experiment also demonstrated increase in RNA synthesis,

as compared to the vivarium control, but to a lesser extent (17%) than after the flight.

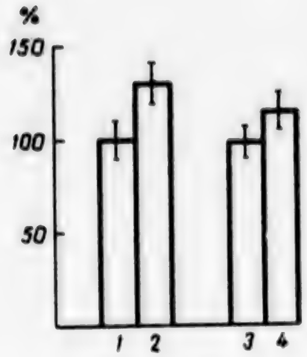

Figure 1.
Endogenous RNA synthesis in hepatic nuclei

Y-axis--incorporation of ^{3}H-UMP
1) control for flight group
2) flight group
3) control for synchronous experiment
4) synchronous experiment

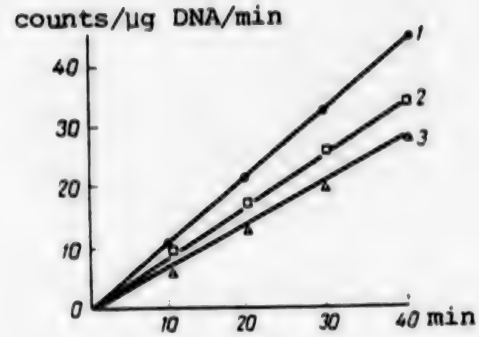

Figure 2.
Kinetics of ^{3}H-UMP incorporation in RNA polymerase system

X-axis--incubation time at 30°C (1 min);
y-axis--incorporation of ^{3}H-UMP (counts/µg DNA/min)
1) flight
2) synchronous experiment
3) intact control

Figure 2 illustrates the results of testing activity of solubilized DNA-dependent RNA polymerase. It should be noted that this figure uses the same curve for the flight and synchronous experiment controls, since they coincided in absolute values in this case. The illustrated data warrant the conclusion that incorporation of ^{3}H-UMP in RNA is higher in flight animals than in the synchronous experiment and control.

Addition of α-amanitin (a specific inhibitory of RNA polymerase II) to the incubation medium depressed label uptake to about the same extent in the experiment and control (by 47 and 50%). Consequently, enzyme activity remained higher in the flight group than in the control with and without the inhibitor. This warrants the belief that the increased activity in the flight variant is attributable to both forms of the enzyme (RNA polymerase I and RNA polymerase II), which synthesize precursors of ribosomal and template RNA, respectively. Thus, changes were observed in enzyme activity of experimental animals that were analogous in direction to those noted for endogenous RNA synthesis in nuclei, and they were manifested by an increase in RNA-synthesizing activity of the liver of animals flown in space.

Changes in transcription of hepatic cells, which were noted in this study, can be interpreted from the standpoint of conceptions of the mechanism of action on the genetic system of glucocorticoid hormones [1]. RNA synthesis is intensified in the liver under the influence of glucocorticoids that are released in stress situations. Activation of transcription in hepatocyte nuclei corresponds to a stress response of the genetic system of liver nuclei at the landing stage, and it is probably similar in nature. Considering the data about intensification of RNA-synthesizing activity in the liver of flight animals, it can be concluded that the observed tendency toward a

decline in concentration of nucleic acids is attributable to other causes, for example, hyperfunction of the cytoplasmic systems of cells, including protein-synthesizing activity, aimed at activation of a number of enzymes that are of importance to adaptation [4].

Our findings indicate that the response of the RNA-synthesizing system of liver cells to a brief spaceflight (7 days) is analogous in direction to the reaction we observed previously to longer spaceflights (18 days), and it consists of increase in RNA-synthesizing activity.

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ROLE OF OPTOKINETIC STIMULATION IN VESTIBULOSPINAL REFLEXES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 8 Dec 86) pp 36-41

[Article by Yu. V. Krylov, V. V. Ivanov, A. A. Podshivalov and V. V. Zaritskiy]

[English abstract from source] This paper presents data about the effect of optokinetic stimulation (OKS) on vestibulospinal reflexes and discusses mechanisms of interaction of the vestibular, optic and proprioceptive sensors during their combined stimulation. The vestibulospinal reflexes were investigated using a 2-minute step test and simultaneous OKS that was produced on the head of the test subject. During the tests optokinetic nystagmus was recorded and the angle of body rotation relative to the initial position was measured. It was found that during the step test the body turned along the OKS direction, i.e. towards the slow component of optokinetic nystagmus. During leftward OKS the angle of rotation was larger than during rightward OKS: 406.4±75.9 deg and 207.5±40.7 deg, respectively. During leftward OKS loss of equilibrium was recorded 4.5 times oftener than during rightward OKS. It has been demonstrated that the capacity to track stimuli moving to the left is lower than that to pursue stimuli moving to the right. It has been shown that there is a correlation between the rate of the optokinetic nystagmus slow phase and the angle of body rotation during the step test. It has been concluded that optokinetic nystagmus can be used as an informative parameter when measuring statokinetic stability in response to multisensory stimulation.

[Text] Pilot and cosmonaut work involves constant analysis of information that is received as a result of inspecting intra- and extra-cabin space, perception of accelerations of the flight vehicle and pressure applied to the controls [10]. Coordinated function of the visual, vestibular and proprioceptive analyzers under complicated dynamic flight conditions acquires particular importance to successful performance of professional tasks. Malcoordination of the function of these analyzer systems could lead to change in motor coordinations that are the basis of work movements [4]. The mechanism of interaction between the vestibular and proprioceptive sensory systems has been investigated thoroughly, whereas the role of visual afferentation in reactions based on vestibulospinal reflexes has not been sufficiently identified.

It is known that altered visual afferentation could lead to modification of neuroreflex associations in formation of animal reflexes upon which equilibrium is based [4, 5, 11]. By assessing the nature of vestibulosomatic responses, a particular manifestation of which is referable to vestibulospinal reflexes, one can determine the functional state of the equilibrium system [4]. The step test (ST) after Fukuda [14], which is used extensively in vestibulometric practice, is one of the easiest and informative methods of studying vestibulospinal reflexes in implementation of complexly coordinated movements.

However, there are only a few studies involving polysensory stimulation in investigating the role of the somatic component in the structure of interaction between the visual and vestibular analyzers. Such relations were analyzed [3, 14] during the ST with optokinetic stimulation (OKS). In particular, it was proposed to objectively determine the effect of altered visual afferentation on vestibulospinal reflexes according to extent of body turn during the ST following OKS. It was shown that, during walking, most subjects turned their body in the opposite direction from OKS [3]. Tests performed with the ST with eyes open in a rotating optokinetic drum revealed disturbances in spatial orientation, the severity of which depended on intensity of OKS [14].

In previous studies, no details were obtained on the mechanisms of effect of oculomotor responses on muscles of the extremities and drunk, which are the effector component of vestibulospinal reflexes.

Our objective here was to test the influence of OKS on vestibulospinal reflexes and to identify some of the mechanisms of interaction between the vestibular, visual and proprioceptive analyzers.

Methods

These studies were conducted on 23 volunteer subjects ranging in age from 19 to 30 years. To objectivize the extent of OKS effect on vestibulospinal reflexes, we measured the angle of body turn while walking in place at the rate of 100 steps/min for 2 min with both eyes shut and OKS. Each test consisted of 4 ST at 3-min intervals. The subjects were divided into two groups. In the 1st group (12 people), the tests were performed in the following order: ST with the eyes closed, ST with OKS to the right, then ST with OKS to the left and again ST with the eyes closed. In the 2d group, after the test with the eyes closed, ST with OKS was performed with optic stimulation to the left and then to the right. OKS during the ST was delivered by means of a special device (Figure 1), which was developed by V. V. Ivanov, Yu. F. Bondarev and O. N. Vasilyev. This device consisted of an optokinetic drum, actuated by an electric motor secured on the helmet, a governor to rule out extraneous visual stimuli, device to illuminate the optokinetic drum on the inside, and a power unit. The drum was rotated at the rate of 60°/s. We recorded optokinetic nystagmus by the method of A. Ye. Kurashvili and V. V. Babiyak on a Mingograf-81 instrument for 10 s prior to the ST with OKS and continuously during walking. During the test, we determined the total angle of body turn from the baseline position. We calculated the velocity of the slow phase (SPV) of optokinetic nystagmus (OKN) as one of the most informative criteria for its evaluation [9]. The obtained data were submitted to statistical

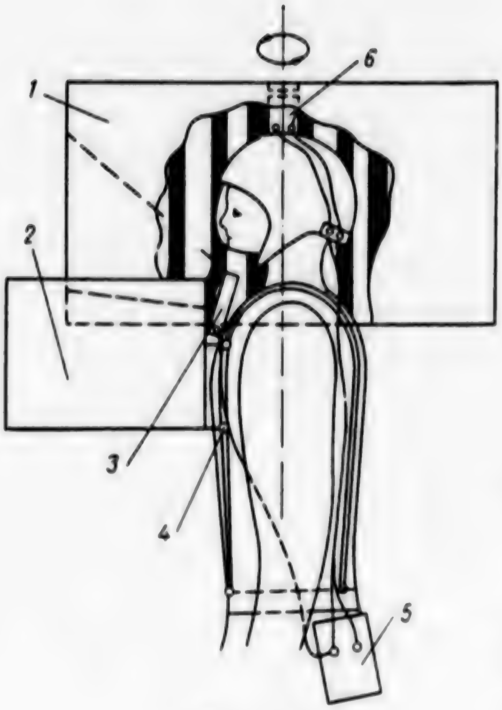

Figure 1.
Device for OKS
1) optokinetic drum
2) visual field limiter
3) lighting device
4) attachment system
5) electric power unit
6) electric motor

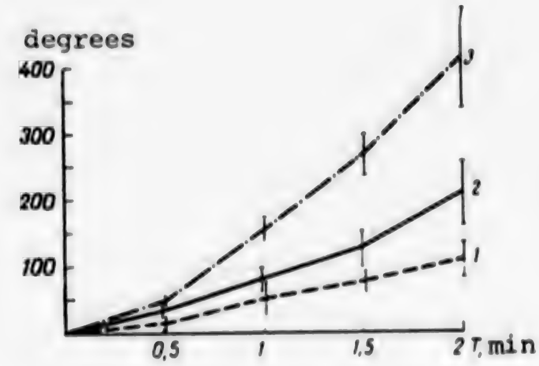

Figure 2.
Body turns during ST
1) without OKS
,3) with OKS to the right and left, respectively

processing using the parameteric criterion of Student (P_t) and nonparameteric criterion of Wilcoxson-Mann-Whitney (P_u)

Results and Discussion

It was established that there was a body turn to the right in 19 subjects during ST with OKS to the right, left body turn in 3 subjects, and only 1 subject performed the test without turning his body. The results of ST with OKS to the left were the exact opposite of those observed with OKS to the right: turn to the left in 19 cases, to the right in 3 and no turn in 1 case. The overall angle of deflection with OKS to the right constituted 207.5±40.7°, and with OKS to the left it was 406.4±75.9° ($P_t<0.05$). The order in which OKS direction was alternated during ST did not have an appreciable effect on magnitude of turning angle.

Analysis of the results of ST with OKS revealed that the latter has an appreciable effect on vestibulospinal reflexes, as indicated by the fact that 82.6% of the subjects turned their body in the same direction as OKS. The angles of body turns during ST with OKS were considerably larger than during the ST with the eyes closed (Figure 2). The demonstrated deflection of the subjects in the direction of OKS during the ST confirms the finding reported by K. L. Khilov of coinciding vectors of animal reflexes and oculomotor responses.

V. V. Baranovskiy and I. D. Semikopnyy [3], who performed the ST with the eyes shut following OKS, reported that the subjects turned in the opposite direction from OKS. Evidently, this is related to the fact that, under these conditions, postoptokinetic nystagmus is observed, the slow component of which is toward

the opposite direction from prior OKS. Tonic reflexes of trunk and extremity muscles, which are determined by the direction of the slow component of post-optokinetic nystagmus, led to a turn of the subjects' body in the opposite direction of prior OKS.

Illusions of counterrotation were observed in 30% of the subjects during the ST with OKS; they consisted of the sensation that the drum stopped and that they were rotating in the opposite direction. Such illusions had also been observed by other researchers in an optokinetic drum [2, 10, 11]. During the ST with OKS, most subjects experienced instability upon walking, which was associated with some spatial disorientation, while 26% lost their equilibrium, and these disturbances were noted 4.5 times more often with OKS to the left than to the right.

Before the ST, SPV parameters of OKN were somewhat lower with OKS to the left than to the right: 31.40±2.62 and 37.51±2.23°/s, respectively. During the ST, parameters of OKN SPV diminished, constituting 30.96±1.18 to the left and 35.94±2.10°/s to the right ($P_u < 0.05$).

The findings are indicative of the appreciable influence of OKS on vestibulo-spinal reactions, the possible physiological mechanisms of which are illustrated in Figure 3. Thus, with OKS in the process of formation of vestibulospinal reflexes there is involvement of impulsation from optic and oculomotor centers effected via the vestibular nuclei and cerebellum [1].

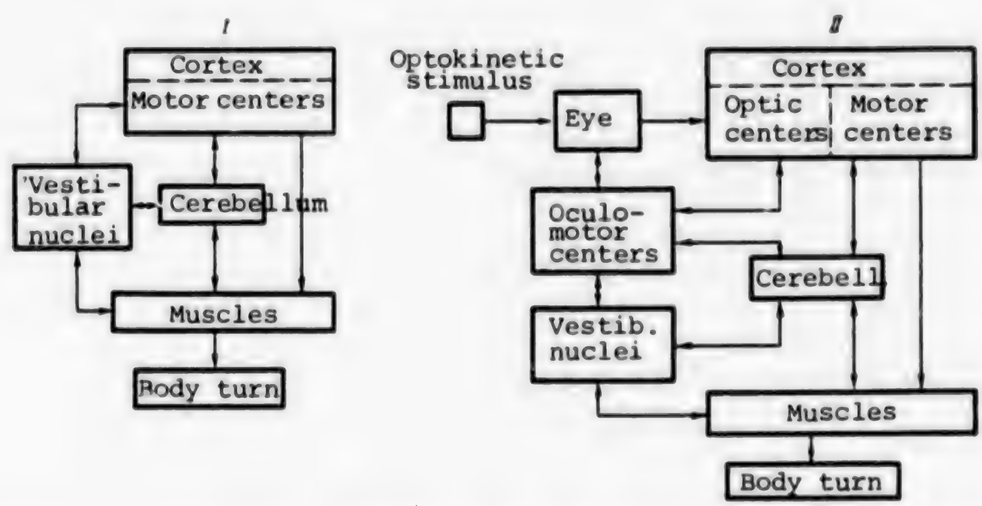

Figure 3. Functional diagram of routes of formation of body turns during ST with the eyes shut (a) and during OKS (b) [evidently shown as I and II in this figure]

The disturbances demonstrated during our tests with reference to spatial orientation and coordination, appearance of illusions of counterrotation are consistent with the data obtained by other researchers. The increase in turn angles and unstable walking were more marked with OKS to the left than to the right. This is perhaps related to more intensive stimulation of the optic analyzer with

OKS to the left. The results of these studies indicate that functional capacity for tracking stimuli moving to the left was lower than for stimuli moving to the right, which is consistent with the early decompensation of tracking when testing tracking motions of the eyes when moving them to the left, as compared to movement to the right [6]. It can be assumed that the decrease in SMP of OKN augments stimulation of the retina and ultimately intensifies the integral effect of stimulation of the visual analyzer through vestibular structures on intensity of vestibulospinal reflexes. Figure 4 illustrates one of the possible mechanisms of this phenomenon.

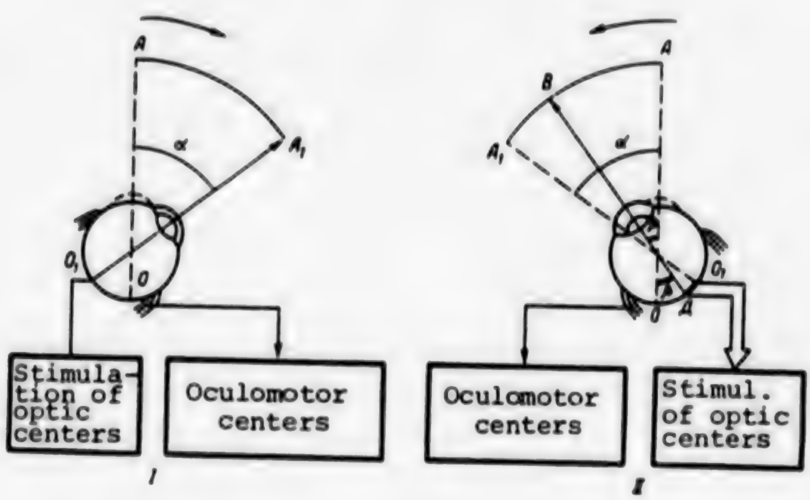

Figure 4. Mechanisms of stimulation of visual analyzer with OKS to the right (I) and to the left (II)

AO) baseline position of optic axis

AA_1) shift of optic stimulus at constant angular velocity ω by angle α; position I: shift of visual stimulus AA_1 by angle α corresponds to shift of optic axis AO to position A_1O_1; position II: shift of visual stimulus AA_1 by angle α does not correspond to shift of optic axis AO to position A_1O_1

ВД) actual position of optic axis

$OД_1$) shift of projection of moving stimulus on retina

β) angle of rotation of eyeball

Thus, when the velocity of the slow phase of OKN and, consequently, the functional capacity of the eye for tracking moving stimuli are rather high, when the optic stimulus is shifted from point A to point A' the eye turns by $\angle\alpha$ and its axis of vision is closest to the O'A' axis (see Figure 3, I). The same retinal field is stimulated here. If, however, the velocity of the slow phase of OKN is much lower than the velocity of OKS, the eye turns by $\angle\beta$ and does not have time to track the stimulus turning by $\angle\alpha$. As a result, the axis of vision ВД will not occupy position A'O' and there will be shifting of the projection of the moving stimulus along the periphery of the retina to a distance ДO' (see Figure 4, II). Thus, the SPV of OKN is an important indicator of the functional capacity of the visual analyzer for tracking moving stimuli. Consequently, high values for OKN SPV provide for stable tracking of

moving objects; decline of OKN SPV leads to greater stimulation of retinal periphery, which causes inadequate optic-vestibular influences on coordination of movements and spatial orientation. This is confirmed by the existing data to the effect that individuals with high OKN SPV are more resistant to optic-vestibular stimulation [2]. The significance of stimulation of peripheral regions of the retina is confirmed by electrophysiological studies, which showed that stimulation of the retinal periphery with moving stimuli alters electrical activity of vestibular nuclear neurons [13]. It was reported that OKS of expressly the peripheral visual fields elicits distinct sensory and autonomic disorders [4, 12]. An increase in sensory perceptions and impaired coordination of movements during OKS were noted [14] in cases where OKN SPV were below the velocity of rotation of the optokinetic drum.

Consequently, optokinetic nystagmus reflects the functional capacity of the visual analyzer for tracking objects moving in the field of vision, while the velocity of the slow phase of this nystagmus is a rather informative criterion that permits determination of the intensity of effect of OKS on distinctions of formation of vestibulospinal reflexes.

Thus, the obtained results lead us to conclude that OKN may be one of the main parameters in determination of statokinetic resistance of man in the presence of polysensory stimulation.

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MEMBRANE MODEL OF CUPULA OF VESTIBULAR SEMICIRCULAR CANALS

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[Article by A. V. Kondrachuk, A. A. Shipov and S. P. Sirenko]

[English abstract from source] A mathematical model of the time-course variations of the cupula of the semicircular canals of the vestibular apparatus is presented. The model is found to be in good agreement with experimental data which suggests that the cupular matter has viscosity-elasticity properties. Their role in the functioning of the vestibular apparatus is discussed in qualitative terms. The applicability of the membrane model to the description of the time-course variations of the cupula is considered.

[Text] It is impossible to comprehend the chain of events that lead to systemic reactions in a dynamic environment without analyzing the function of the vestibular system (otoliths, semicircular canals) under such conditions.

For 5 decades, researchers adhered to the Steinhauzen model [4] in considering physiological responses related to the function of the semicircular canals; this model is a generalization of direct observations of cupular movement under experimental conditions. In spite of a number of simplifications, this model expresses the substance of the principle of cupuloendolymphatic system (CES) function: when the head turns in the plane of the canal, the endolymph is shifted by inertia in relation to its walls, the cupula is deflected from its neutral position, and this is what is recorded by the central nervous system as a turn. Steinhauzen proposed that the dynamics of CES be described with an equation for a supercritically damped one-dimensional harmonic oscillator. It was assumed that the magnitude of viscous friction is determined by the friction of endolymph against the canal surface and that the coefficient of elasticity is determined by the elastic attachment of the cupula on the crista.

Dittrich [10], who made a comprehensive analysis of Steinhauzen's observations, called attention to the deformation (bulging) of the cupula with slight shifts of endolymph, attributing the main physiological significance in spontaneous movements to expressly this cupular reaction. A deviation or shift of the

entire cupula in the crista [11] occurs, according to Dittrich's hypothesis, only when there are nonphysiological (traumatic) angular accelerations. He was the first to compare the cupula to a membrane attached along the edges.

In the 1970's, experimental facts were accumulated that were inconsistent with Steinhauzen's conceptions of the cupula as a "swinging door" [2, 11-13, 21-24], as well as information indicative of the validity of a membrane model of the cupula [15-18, 21]. According to these studies, the cupula is a membrane (diaphragm) that seals the ampulla. However, no connections were found between the lateral surfaces of the cupula and ampulla. There is a subcular space between the cupula and crista. The cupula is stricturally linked with the crista surface, but the subcupular space allows for rather free movement of the lower part of the cupula in relation to the crista upon spontaneous movements of the pendulum type [25]. The apex of the cupula begins to move when the central part of the cupula reaches maximum shifting. Consequently, the hypothesis that there is one-dimensional movement of the cupula, which leads to the mathematical model of Steinhauzen, is an appreciable oversimplification. Indeed, it is not the deflection or movement of the cupula as a whole that is physiologically relevant, but the inclination (shift) of only the base of the cupula adherent to the crista. In order to determine the magnitude of this incoination as a function of an exogenous factor (angular acceleration) one must specify the spatial structure of the cupula, its physical characteristics, nature of attachment on the crista and ampullar walls and relate its behavior with endolymph movement, and it is necessary to consider the distinctions of endolymph interaction with the canal walls and spatial structure of the canal. On this basis, one can assume that it is not a one-dimensional model of cupular movement, but a model that considers its spatial structure that must be used, which corresponds to a change from a system with concentrated parameters to a system with distributed parameters.

A membrane model of the cupula, which reflects the spatially distributed nature of the system is closer to a description of actual behavior of the CES, that corresponds to the usual physiological range of accelerations than the "swinging door" model.

A membrane model of the cupula had been used before [8, 9]; however, this was done without discussing the criteria for its applicability. One author [8] limited himself only to analysis of a special instance of exogenous acceleration, whereas in another study [8], which was a development of [8], attention was focused mainly on determination of endolymph pressure in a semicircular canal with variable cross-section. The authors who formulated a spatially heterogeneous problem then reduced it to an equation with concentrated parameters of the Steinhauzen equation type, and thus there was unjustified loss of information concerning the behavior of the base of the cupula adjacent to the sensory epithelium.

It is interesting to systematically scrutinize a membrane model of the cupula, compare it to experimental data [18] and analyze the conditions of applicability of such a model.

Mathematical model. Let us assume that the semicircular canal is a torus filled with homogeneous, viscous, incompressible fluid (endolymph) with density ρ. The cross-section of the torus overlaps the membrane (cupula) whose

thickness is h; the density of membrane substance and canal fluid is the same. Considering the actual parameters of the SC [semicircular canal], one can consider that there is laminar flow of fluid during physiological movements.

Let us also assume that the presence of a membrane covering the cross-section of the canal does not disrupt laminarity of fluid flow. Given these assumptions, the equations describing dynamics of fluid and membrane have the following appearance:

$$\frac{\partial v}{\partial t} = \nu_\Delta v - \frac{1}{\rho}\frac{\partial p}{\partial z} - \gamma(v) R \dot{\omega}(t), \quad (1)$$

$$\frac{\partial^2 u}{\partial t^2} = \frac{T}{\rho h}\Delta u + \frac{\delta p}{\rho h} - \gamma(v) R \dot{\omega}(t), \quad (2)$$

where ν is the kinematic coefficient of fluid viscosity, u is deflection of the membrane, v is velocity of fluid, p is pressure, δp is pressure gradient on the membrane, $\dot{\omega}(t)$ is the projection of the vector of angular acceleration on the axis perpendicular to the torus plane, T is tension per unit length of membrane perimeter, $\Delta = \frac{1}{r}\frac{\partial}{\partial r} r \frac{\partial}{\partial r}$, where r changes from 0 to r_0 (r_0 is height of cupula), $\gamma(v) = \begin{cases} \gamma, & v \neq 0 \\ 1, & v \neq 0 \end{cases}$ is a coefficient the meaning of which will be discussed below.

By integrating equation (1) for z in the range of 0 to l (l is canal length), considering that $\frac{\partial u}{\partial t} = v$ (3) for incompressible fluid, we shall have:

$$\delta p = \rho l \left\{ -\frac{\partial^2 u}{\partial t^2} - \gamma(v) R \dot{\omega}(t) + \nu \Delta \frac{\partial u}{\partial t} \right\}. \quad (4)$$

Inserting (4) in equation (2), we shall obtain the formula describing movement of the membrane-fluid system:

$$\frac{\partial^2 u}{\partial t^2} = \Delta\left(D_1 u + \nu_1 \frac{\partial u}{\partial t}\right) - \gamma(v) R \dot{\omega}(t), \quad (5)$$

where $D_1 = \frac{T}{\rho(l+h)}$, $\nu_1 = \frac{\nu l}{l+h}$.

Let us find the solution to equation (5) under the following initial and boundary conditions:

$$\left.\frac{\partial u}{\partial t}\right|_{t=0} = v_0(r); \quad u\Big|_{t=0} = u_0(r); \quad u\Big|_{r=r_0} = 0;$$

$$\left.\frac{\partial u}{\partial r}\right|_{r=0} = 0.$$

Let us apply Laplace's transform to equation (5):

$$\Delta u_1 - k^2 u_1 = \frac{F(r, s)}{(D_1 + \nu_1 s)^2}, \qquad (6)$$

where $u_1 = u^* - \frac{\nu_1}{D_1 + \nu_1 s} u_0(r)$, $u^* =$

$= \int_0^\infty e^{-st} u\, dt$, $k = \frac{S}{\sqrt{D_1 + \nu_1 S}}$,

$F(r, s) = (D_1 + \nu_1 s)\{RW - v_0(r)\} -$

$- s D_1' u_0(r)$, $W = \int_0^\infty e^{-st} \gamma(v)\, \omega(t)\, dt$.

The solution for equation (6) will have the following appearance:

$$u_1 = \frac{1}{(D_1 + \nu_1 s)^2} \int_0^{r_0} G(r, \eta) F(\eta, s)\, d\eta,$$

where $G(r, \eta) = \sum_{m=1}^{\infty} \frac{2\eta I_0(k_m \eta) I_0(k_m r)}{r_0^2 (K^2 - K_m^2) I_1^2 (K_m r_0)}$ --

is Green's function, $I_0(k_m \eta)$ is Bessel function of an imaginary argument, are the roots of the equation $I_0(k_m r_0) = 0$, which are related to the roots of real argument $J_0\left(\lambda_m \frac{r}{r_0}\right)$ through $k_m = -i\frac{\lambda_m}{r_0}$.

Thus,

$$u^* = \frac{\nu_1 u_0(r)}{D_1 + \nu_1 s} - \sum_{m=1}^{\infty} \times$$

$$\times \frac{2 J_0\left(\lambda_m \frac{r}{r_0}\right)}{r_0^2 J_1^2(\lambda_m)\left(s - s_m^{(1)}\right)\left(s - s_m^{(2)}\right)(D_1 + \nu_1 s)} \times$$

$$\times \int_0^{r_0} \eta J_0\left(\frac{\lambda_m}{r_0}\eta\right) F(\eta, s)\, d\eta \qquad (7)$$

where $s_m^{(1),(2)}\ \frac{\lambda_m^2}{r_0^2}\left(-\frac{\nu_1}{2} \pm \sqrt{\frac{\nu_1^2}{4} - \frac{r_0^2}{\lambda_m^2} D_1}\right)$.

Having applied the formula for handling Laplace transform to equation (7) and using the convolution theorem, we shall obtain the solution to equation (5) in the following form:

$$u=\sum_{m=1}^{\infty}\frac{2J_0\left(\lambda_m\frac{r}{r_0}\right)}{r_0^2J_1\left(\lambda_m\right)\left(S_m^{(1)}-S_m^{(2)}\right)}\int_0^{r_0}\eta\left\{\left[v_0(\eta)-S_m^{(2)}u_0(\eta)\right]e^{S_m^{(1)}t}+\right.$$
$$\left.+\left[s_m^{(1)}u_0(\eta)-v_0(\eta)\right]e^{S_m^{(2)}t}\right\}J_0\left(\frac{\lambda_m}{r_0}\eta\right)d\eta-\gamma(v)R\sum_{m=1}^{\infty}$$
$$\frac{2J_0\left(\lambda_m\frac{r}{r_0}\right)}{\lambda_mJ_1\left(\lambda_m\right)\left(S_m^{(1)}-S_m^{(2)}\right)}\int_0^{t}\left(e^{S_m^{(1)}(t-\tau)}-e^{S_m^{(2)}(t-\tau)}\right)\dot{\omega}(\tau)\,d\tau. \qquad (8)$$

Since the CES is damped supercritically $\left(\frac{\nu_1^2}{4}>\frac{r_0^2}{\lambda_m^2}D_1\right)$ and the terms of expanding (8) rapidly diminish as m increases, the approximate solution of equation (5) can be submitted in the following form:

$$u\simeq\frac{2J_0\left(\lambda_1\frac{r}{r_0}\right)}{r_0^2J_1^2\left(\lambda_1\right)}\int_0^{r_0}\eta\left\{\tau_1v_0(\eta)\left(e^{-\frac{t}{\tau_2}}-e^{-\frac{t}{\tau_1}}\right)+\right.$$
$$\left.+u_0(\eta)e^{-\frac{t}{\tau_2}}\right\}J_0\left(\frac{\lambda_1}{r_0}\eta\right)d\eta-\gamma(v)R\times$$
$$\times\frac{2J_0\left(\lambda_1\frac{r}{r_0}\right)}{\lambda_1J_1\left(\lambda_1\right)}\tau_1\int_0^{t}\dot{\omega}(\tau)\left(e^{-\frac{t-\tau}{\tau_2}}-e^{-\frac{t-\tau}{\tau_1}}\right)d\tau, \qquad (9)$$

where $\tau_1=\frac{r_0^2}{\lambda_1^2\nu_1}$ is the fast-time constant (10), $\tau_2=\frac{\nu_1}{D_1}$ is the slow-time constant (11).

The product of r at point r_0 of equation (9) taken with the opposite sign determines the angle of deflection of the membrane at the attachment site. This angle can be equated to the angle of deflection of sensory cell hairs:

$$\xi=\frac{2\lambda_1}{r_0^3J_1\left(\lambda_1\right)}\int_0^{r_0}\eta\left\{u_0(\eta)e^{-\frac{t}{\tau_2}}+\tau_1v_0(\eta)\times\right.$$
$$\left.\times\left(e^{-\frac{t}{\tau_2}}-e^{-\frac{t}{\tau_1}}\right)\right\}J_0\left(\frac{\lambda_1}{r_0}\eta\right)d\eta-\frac{2\gamma(v)R\tau_1}{r_0}\times$$
$$\times\int_0^{t}\left(e^{-\frac{t-\tau}{\tau_2}}-e^{-\frac{t-\tau}{\tau_1}}\right)\dot{\omega}(\tau)\,d\tau. \qquad (12)$$

Let us examine the reaction of the cupular membrane to two types of exogenous factors:

1. Stop-stimulus. Assuming that:

$$v_0(r) = 0,\ u_0(r) = 0,\ \omega(t) = \begin{cases} \omega = \text{const},\ t<0 \\ 0,\ t>0 \end{cases}$$

we shall have:

$$u = -\gamma \frac{2R J_0\left(\lambda_1 \frac{r}{r_0}\right)}{\lambda_1 J_1(\lambda_1)} \tau_1 \omega \times$$

$$\times \left(e^{-\frac{t}{\tau_2}} - e^{-\frac{t}{\tau_1}}\right), \qquad (13)$$

hence

$$\xi = -\gamma \frac{2R}{r_0} \tau_1 \omega \left(e^{-\frac{t}{\tau_2}} - e^{-\frac{t}{\tau_1}}\right). \qquad (14)$$

Thus, deflection of the hairs (inclination of cupula) will reach a maximum in time $t \ll \tau_1$:

$$\xi_{max} = -\gamma \frac{2R}{r_0} \tau_1 \omega,$$

$$u_{max} = -\gamma \frac{2R\tau_1\omega}{\lambda_1 J_1(\lambda_1)} J_0\left(\lambda_1 \frac{r}{r_0}\right),$$

and with $t \gg \tau_2$ it strives toward zero.

2. Periodic factor. Assuming that $\dot{\omega}(t) = \tilde{\omega}^2 A \sin\tilde{\omega}t$, with $t \to \infty$ and $\tilde{\omega}\frac{1}{\tau_1}$, we shall obtain:

$$u = -\gamma \times$$

$$\times \frac{2R\tau_1\tau_2 A\tilde{\omega}^2 J_0\left(\lambda_1 \frac{r}{r_0}\right)}{\lambda_1 J_1(\lambda_1)\sqrt{1+\tilde{\omega}^2\tau_2^2}} \sin(\tilde{\omega}t - \varphi), \qquad (15)$$

hence,

$$\xi = -\gamma \frac{2R\tau_1\tau_2 A\tilde{\omega}^2}{r_0\sqrt{1+\tilde{\omega}^2\tau_2^2}} \sin(\tilde{\omega}t - \varphi), \qquad (16)$$

where $\tilde{\omega}$ is the cyclic frequency of harmonic oscillations of the CES, φ is the phase difference between ξ, u and $\dot{\omega}(t)$, and

$$\operatorname{tg}\varphi = \frac{\tilde{\omega}\tau_2}{1 - \tilde{\omega}^2\tau_1\tau_2}. \qquad (17)$$

Comparison to experimental data. Discussion

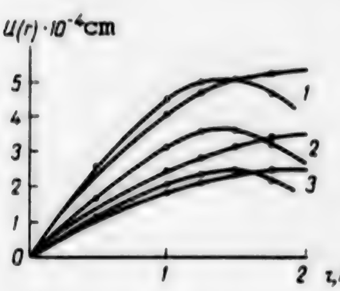
We are dealing here with a SC model in the form of a torus with unchanging cross-section. However, the cross-section of an actual semicircular canal is a variable. For this reason, when the CES is exposed to dynamic factors, movements of the cupula in the ampulla are smaller than the movements of endolymph in the narrow part of the canal. Let us introduce in equations (1) and (2) coefficient $\gamma(v)$, which reduces shifting of the cupula, and thus let us consider the influence of geometric heterogeneity of the canal's cross-section on cupular dynamics. For incompressible endolymph, the ratio between average movements of the cupula in the ampulla and endolymph in the narrow part of the canal should be approximately equal to the square of the ratio of the radius of canal cross-section to half the height of the cupula. This ratio will be the estimate of γ. Since half the height of the cupula r_k equals approximately 0.03 cm* [19], $\gamma = 0.2$. It should be noted that $\gamma(v) = \begin{cases} \gamma, & v \neq 0 \\ 1, & v = 0 \end{cases}$ because in the static case fluid pressure on the cupula does not depend on geometric heterogeneity of canal cross-section. One can be readily convinced of this by integrating the Navier-Stokes equation with $v = 0$. The pressure gradient for endolymph on the cupula determined in this manner, $\delta p = \rho R \dot{\omega} l(\dot{\omega} = \text{const})$ depends only on angular acceleration and length of the region occupied by endolymph. It must be stressed that this approximate conception imposes some restrctions on the CES model, in particular, it does not allow us to observe the change in CES from dynamic to static state when this system is exposed to a constant inertial force.

Let us assess the slow and fast time constants of the CES system. With $\tilde{\omega} = 4.7\ s^{-1}$, $\varphi = 64°$ [18], $\nu = 10^{-2}\ cm^2/s$ [9, 16], $r_0 = 0.014$ cm, R = 0.14 cm [4] and $\lambda_1^2 = 5.78$, according to formulas (10) and (15) we find that $\tau_1 = 3.4 \cdot 10^{-3}$ s and $\tau_2 = 0.4$ s.

Using the obtained estimates for τ_1, τ_2, γ and formula (15), let us plot the profile of the cupula at specified points in time during sinusoidal rocking of the CES (Figure 1). A comparison of the theoretical profile to the one observed in the experiment [18] shows that they are in rather good agreement. Deviation of the nominal curves from the experimental ones in the right part of the graph is probably related to the fact that cupular thickness h is a variable, rather than a constant, as it was assumed in deriving the equation of membrane movement and, furthermore, its shape is other than a circle.

The slow time constant $\tau_2 = 0.4$ s calculated from the results of the study with sinusoidal oscillation of the cupula ($\tilde{\omega} \approx 5\ s^{-1}$) [18] is smaller by a factor of 10^2 than the value obtained in [13] where the time of return of the cupula to an equilibrium position after the shift was recorded ($\tau_2 \sim 10$ s, $\tilde{\omega} \sim 0$). Hence, it can be concluded that with increase in oscillation frequency the slow time constant diminishes. An analogous conclusion can be derived from analysis of the results in [6], a study in which the activity of individual fibers of the ampullar nerve was recorded during oscillation at a different frequency. Indeed, with $\tilde{\omega} = 6.28\ s^{-1}$ ($\varphi = 64$–$80°$), we have $\tau_2 = 0.3$–0.8 s; with $\tilde{\omega} = 0.31\ s^{-1}$ ($\varphi = 45$–$63°$), we have $\tau_2 = 3.2$–6.2 s.

*All of the calculations in this article were made for the CES of the giant bullfrog.



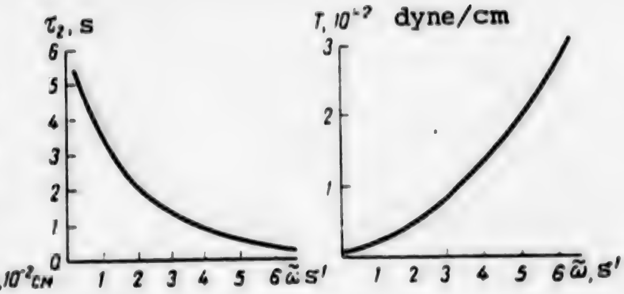


Figure 1.
Characteristic curves of cupular deflection
X-axis, distance from crista to apex of cupua; y-axis, amplitude of cupular deflection. Curves 1-3 refer to velocities of 3.4, 2.4 and 1.6 rad/s of periodic factor
o--theoretical points (formula 15)
•--experimental points (17)

Figure 2.
Slow time constant of CES τ_2 and tension coefficient T as a function of periodic factor ω, calculated using formulas (17) and (11) on the basis of experimental data [5]

The decline of $\tau_2 = \frac{\nu_1}{D_1}$ with rise in frequency of exogenous oscillation signifies an increase in cupular coefficient of elasticity (Figure 2), and this, in turn, enables us to assume that the cupula is a viscoelastic structure. To verify this assumption, it is necessary to perform experiments with visualization of movement of the cupula in the oscillation range of 0.1-1 s^{-1}, as well as to estimate the physical parameters of the cupula.

Let us discuss the possible physiological interpretation of the viscoelastic behavior of the cupula. According to formulas (15) and (16), with $\tilde{\omega}\tau_2<1$ the CES has a differential property, since in this case deflection of the cupula (bending of hairs) is proportionate to acceleration $\dot{\tilde{\omega}}(t)$ of the exogenous factor. With $\tilde{\omega}\tau_2>1$, the CES has an integral property (ξ, $u \sim A\tilde{\omega}$). Evidently, under ordinary conditions the CES functions in the integration mode, since it is exposed mainly to rapidly changing inertial forces. In the range of low frequencies, condition $\tilde{\omega}\tau_2>1$ is met if τ_2 is high enough, which corresponds to a low CES elasticity factor. However, by definition τ_2 has the meaning of intrinsic time of system recovery [formulas (13), (14)] and should be rather low in value (and the elasticity factor should be rather high) when the CES is exposed to high-frequency stimuli. A compromise between these two requirements is obtained by τ_2 as a function of $\tilde{\omega}$, i.e., the viscoelastic properties of the cupula. If τ_2 were independent of $\tilde{\omega}$ this integrating property is impaired, according to equation (16), at low frequencies $\left(\tilde{\omega}<\frac{1}{\tau_2}\right)$, and ξ, u would be proportionate to acceleration of the exogenous periodic factor. Thus, an increase in τ_2 in the range of low frequencies, attributable to viscoelasticity of the cupula, makes it possible to widen somewhat the frequency range in which the CES has integrating action. At very low frequencies, the integrative nature of the system would nevertheless be impaired, and this may be one of the causes of vestibular disturbances associated with low-frequency periodic stimuli. If the cupula did not have viscoelastic properties and the slow time constant τ_2 constituted about 10 s [23], the CES [see formula (17)] at frequencies of $\omega>3.2\ s^{-1}$ ($\tau_1\tau_2 \sim 0.1\ s^2$ [23]) would be ahead of the stimulus in phase, which is in contradiction to the experimental data [6, 18]. If the cupula has

viscoelastic properties, the CES functions in a mode of phase lage behind the exogenous stimulus, in the physiological range of frequencies, and this is consistent with the experimental data.

The membrane model of a cupula discussed here is the most elementary one, and the adequacy of its behavior for the actual dynamics of a cupula requires special discussion.

Structurally, the cupula is a plate about 10^{-2} cm thick [23], made of elastic (possible, viscoelastic) substance with very low Young's modulus (10^3 to 10^5 dyne/cm^2, according to different estimates [20, 23]), the density of which is close to that of endolymph [22], and it overlaps the canal. The dynamics of the plate can be approximately described with a membrane equation in the case where a rather large tensile force T is applied to it. The magnitude of tensile force for the cupula is determined by endolymphatic pressure, as well as interaction between the cupular substance and walls of the ampulla, crista and endolymph. Thus, the concept of a cupula as a membrane is consistent with its functional behavior, rather than a description of a real object. For example, there has been insufficient investigation of the nature of cupular attachment along the perimeter. Experimental results [17, 18] indicate that the bottom part of the cupula adjacent to the epithelium bends, rather than slides on it when endolymph pressure is raised. It is assumed that the cupula is in a compressed state and presses against the canal wall through forces of elasticity, since no structural connection has been found between the cupula and ampullar wall. In addition, it was found [18] that the cupular substances is drawn to the ampullar walls because of its adhesive properties. Consequently, the cupula is a rather complex structure and it is a substantial oversimplification to conceive of it in the form of an elastic membrane characterized by a single parameter, tension T.

As we know [3, 5], deflection of a round plate with cross-section radius r_k, Young's modulus E, Poisson coefficient σ, thickness h, submitted to an exogenous tensile force T applied to its edge can be described by the membrane equation in the case where the following condition is met: $\frac{h^3 E}{12(1-\sigma^2) r_k^2} \ll T$. For $h \sim 10^{-2}$ cm, $\sigma \simeq 0.5$, r_k 10^{-2} cm, $\tilde{\omega} = 4.7$ s^{-1}, $\tau_2 = 0.4$ s, $T \sim 10^{-2}$ dyne/cm, we have $E \ll 10$ dyne/cm^2. Consequently, the membrane model is valid for describing a cupula only if there is an exogenous tensile force, under the influence of which the cupula is sort of stretched in the section perpendicular to the axis of the canal, and the value for Young's modulus E must not exceed $T \frac{12(1-\sigma^2) r_k^2}{h^3}$. At the present time, there are no precise data concerning the relevance of Young's modulus E and tensile forces T. However, the role of the latter can be ascribed to capillary forces.

As shown by the above estimates, with a low Young's modulus for cupular substance ($E \leqslant 10$ dyne/cm) a rather low value for $T \sim 10^{-2}$ dyne/cm^2 is sufficient for the cupula to acquire the properties of a stretched membrane. It should be noted that the obtained value for T is close to the values for coefficients of surface tension of a number of biological substances [1].

Thus, in order to determine whether the membrane model of a cupula is adequate, experiments must be conducted to define its elastic and surface properties.

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UDC: 612.821-06:612.232.4

INVESTIGATION OF EFFECTS OF SHORT-TERM EXPOSURE TO HIGH CONCENTRATIONS OF CARBON MONOXIDE ON OPERATOR'S PSYCHOPHYSIOLOGICAL FUNCTIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, Sep-Oct 87 (manuscript received 24 Oct 86) pp 47-50

[Article by V. Ye. Yastrebov, V. V. Kustov and S. M. Razinkin]

[English abstract from source] Experiments on volunteers, aged 26-40, demonstrated that a 10-minute exposure to carbon monoxide at a concentration of 900±20 mg/m^3 caused a significant decline of the quality of their operator's function. The task they performed was a two-dimensional compensatory tracking task combined with mental arithmetics. Some of the test subjects showed symptoms of mild CO intoxication which preceded disorders in their work and were accompanied by an increase of HbCO to 10±0.57%. Such an exposure to CO should be regarded as hazardous since it may increase the probability of erroneous actions, particularly, of the flying personnel.

[Text] Exposure to carbon monoxide (CO) in relatively low concentrations (100-300 mg/m^3), which leads to 4-10% increase in blood carboxyhemoglobin (HbCO), elicits disturbances in several human psychophysiological functions: worsening of psychomotor performance and memory, decline in scope and concentration of attention and others [1, 4-6, 10, 11].

This paper deals with investigation of the consequences of short-term exposure to high concentrations of CO, when compensatory and adaptive mechanisms do not have time to develop.

Methods

We used a model of two-dimensional compensatory tracking with simultaneous continuous performance of additional mental task in order to assess the effect of CO on operator efficiency.

These studies were conducted on 8 volunteer subjects, essentially healthy men 26-40 years of age, 3 of whom smoked. The smokers stopped smoking 4 h before the experiment. The protocol for all of the studies included 5-min work for baseline recordings of psychophysiological parameters and subsequent work for 30 min.

We conducted two series of studies involving eight tests each: 1st series--10-min exposure to CO in a concentration of 900±20 mg/m^3; 2d series (control)--breathing atmospheric air. For these studies a system of graded delivery of CO into the space under the mask was developed. An initial gas-air mixture containing CO in a concentration of about 2000 mg/m^3 was prepared in a 40-ℓ tank; this is the maximum safe level for 10-min inhalation [12]. The mixture was delivered from the tank through a reducing valve and rheometer into a mixing tank, into which purified room air, which was also graded (through a rheometer), was delivered also. The obtain gas-air mixture was collected in Douglas bags and delivered into the space underneath the mask.

Prior to these studies, technical experiments were conducted on volunteers to adjust the nominal CO concentration (about 900 mg/m^3). CO content in the mixture was monitored by linear-colorimetric and photoelectric colorimetric methods [9]. In control studies, the subjects breathed purified room air, but they were not informed of this.

The quality of operator performance was assessed according to integral error and mismatch time for signals during their tracking on a Slezheniye-5 [Tracking] instrument. Concurrently, we determined the rate of processing of additional information in bits/s [3, 7], according to choice between two alternatives: determination of whether the sum of two numbers presented in the peripheral visual field, with use of the Fiziolog-M instrument, was odd or even.

Prior to the tests with CO, all of the subjects underwent training until stable parameters were obtained for quality of performance of combined work. A high level of motivation was obtained by informing the subjects of the nature and importance of the tests and introducing elements of competition in performing test tasks.

During the tests, we made records each minute of the integral of error and mismatch time with respect to signals from two control channels, number of times buttons were depressed in response to presentation of numbers (with separate recording of correct answers), heart rate (HR), respiration rate (RR), respiratory minute volume (MV). Immediately after using CO, in the 16th min of the test, there was a break in tracking work lasting about 1 min in order to draw blood for carboxyhemoglobin testing. Blood samples for HbCO were also drawn prior to the study and immediately after it.

Carboxyhemoglobin content of blood was determined by spectrophitometry [2].

In order to demonstrate any tendency toward change in physiological parameters, we determined the differential oxygen pulse (ΔOP) in relative units using the following formula:

$$\Delta OP = \frac{\Delta MV}{\Delta HR}$$

where $\Delta MV = MV_i - MV_{bl[baseline]}$ and $\Delta HR = HR_i - HR_{bl}$.

We used conventional methods of variation statistics with parameteric and non-parametric criteria.

Results and Discussion

As a result of these studies, it was established that there was reliable ($p<0.05$) increase in error integral and signal mismatch time over the two control channels in three subjects (including one smoker) under the effect of CO. Maximum worsening of these parameters was observed in the 30th min of combined operator work (25 min after start of exposure to CO).

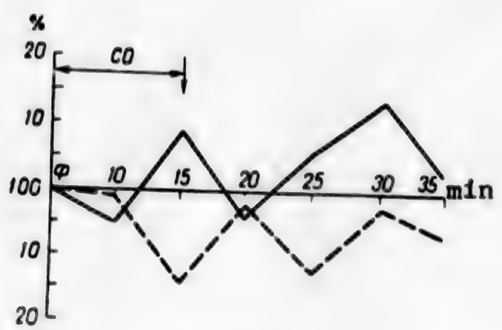

Figure 1.

Change in rate of processing of additional information in operator work while breathing air (boldface line) and mixture of CO and air (dash line)

Here and in Figures 2 and 3: x-axis--working time (min); y-axis, change in speed of information processing; φ--baseline

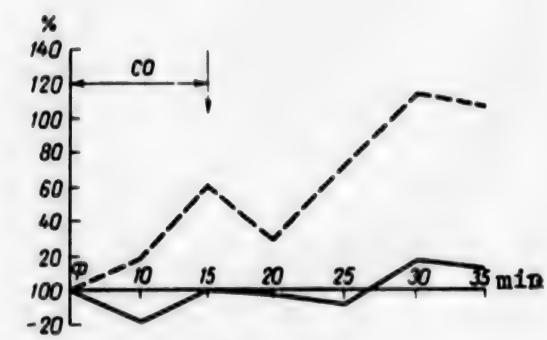

Figure 2.

Change in quality of operator work while breathing air (boldface line) and mixture of CO and air (dash line) Y-axis, $\Delta XY + \Delta T_{xy}$ (%)

There was no change in rate of processing additional information during the experiments ($p>0.05$); however, there was a distinct tendency toward its decline under the effect of CO, as compared to the control (Figure 1).

The error integral and mismatch time for the signals are the two characteristics of the single process of visual and motor operator activity. For this reason, the quality of operator performance can be assessed using a parameter which is the total increment (%) of error integral (ΔXY) and signal mismatch time (ΔT_{xy}) via the two control channels (Figure 2). Figure 2 illustrates the dynamics of change in this overall parameter of operatory performance under the effect of CO and while breathing pure air in a group of three subjects. Maximum difference in operator performance under the effect of CO and in the control is observed in the 30th min of the test and it constitutes 96.5%. Improved performance between the 15th and 20th min of the study can be attributed to the 1-min break after the 15th min of work in order to draw blood for assay of HbCO.

Examination of dynamics of blood HbCO content while subjects performed combined work during exposure to CO revealed the following: baseline HbCO 1.6±0.25%, in 15th min 10±0.57%, and in the control study 8.6±0.59%. Maximum absolute HbCO constituted about 12%.

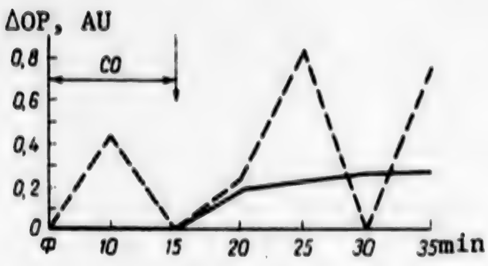

Figure 3.
Adaptation of HR to metabolic level of operator work while breathing air (boldface line) and mixture of CO with air (dash line)
AU) arbitrary units

No reliable differences were demonstrated between recorded physiological parameters with exposure to CO and in the control. In the control, we observed gradual increase in differential oxygen pulse, which is probably related to the presence of some nervous and emotional stress during combined operator work (Figure 3). Under the effect of CO we observed fluctuating changes in ΔOP, which apparently reflects impairment of the body's capacity to reach a response level adequate to the nature of activity.

During combined operator work with exposure to CO, 5 out of 8 subjects complained of heaviness of the head, apathy, sleepiness and difficulties in solving mathematical problems in the 15th-20th min of the test. One of them also complained of headache, while another noticed cooling of the hands. These symptoms can be viewed as a clinical manifestation of mild CO intoxication.

The significant number of subjects with complains and the short period of time from the start of exposure to CO and appearance of subjective sensations (5-10 min) can be attributed to the nature of the work. During combined operator work, due to presence of nervous and emotional tension, there is increase in metabolic processes, in particular in the brain. It can be assumed that, under such conditions, CO elicits more marked relative hypoxia of brain tissue (primarily the cortex) than at rest, as a result of its direct histotoxic action.

This assumption can be voiced if we consider the results of previous studies [8], which showed depression of the process of biological oxidation in cells of the sensorimotor cortex, which is due to the tissular effect of CO.

This investigation warrants the conclusion that exposure to CO in a concentration of 900±20 mg/m^3 elicits worsening of operator performance, with appearance of the clinical signs inherent in mild acute CO intoxication. These circumstances acquire particular importance to flight work. It can be assumed that, under such conditions of exposure to CO, there is increased probability of tracking errors, i.e., continuous sensorimotor (visual-motor) performance, as well as in tasks requiring rapid decision making. This could affect in particular the stages of flight where particular piloting accuracy is required, as well as complicated flying conditions.

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HUMAN BLOOD GLUTAMIC ACID LEVEL WITH EXPOSURE TO HIGH AMBIENT CONCENTRATIONS OF AMMONIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 16 Dec 86) pp 50-52

[Article by V. P. Savina, T. F. Vlasova and Ye. B. Miroshnikova]

[English abstract from source] Amino acid metabolism of men kept in an enclosed environment was investigated. A high concentration of ammonia produced a specific redistribution of free amino acids in plasma, with the content of glutamic acid increasing by the end of the study. The estimates of glutamic acid in blood can be used for assessing maximally allowable concentrations of ammonia in enclosed environments.

[Text] Studies of recent years indicate that parameters of amino acid metabolism, i.e., concentration of free amino acids in plasma, which play a large part in biochemical processesin the body, have some diagnostic significance under clinical conditions and in studies involving man [5, 8, 17, 18]. It should be noted that, in stress situations, a distinctive redistribution of the amino acid pool in blood is observed, which is due to the increased need to furnish the body with energy and plastic materials, and which is apparently due to differentiated utilization of amino acids [1-4, 11, 15, 17]. Our objective here was to determine the integral parameters of amino acid metabolism of man while in a closed environment with alteration of parameters of the gas atmosphere. There are only sparse reports on this score in the literature available to us [2, 10, 20].

Methods

We studied some aspects of amino acid metablism in a closed chamber on four subjects. The study involved two successive stages without interruption. The baseline period lasting 20 days was outside the chamber on an unrestricted regimen while remaining in the hospital around the clock. The after effect period lasted 6 days and the same conditions prevailed. The first stage of the test period lasted 6 days with the subjects remaining in the chamber with the following ambient parameters: mean CO_2 content did not exceed 0.4-0.6%, O_2 content constituted 19% and air temperature was 20±2°C. The second stage period lasted 37 days, during which the subjects remained in the chamber

with ambient parameters analogous to those used at the first stage, but with constantly increasing concentration of ammonia to 2 mg/m^3. The subjects were on a standard diet. Determination of free amino acids in plasma drawn from fasting subjects was made using an automatic analyzer, with margin of error of ±2% [5, 19]. Samples were deproteinized with crystalline sulfosalicylic acid [16]. Venous blood was drawn once in the baseline period, once (on the 6th day) at the first stage of the study, 4 times (on 6th, 13th, 25th and 37th days) at the second stage and once (on 6th day) in the aftereffect period. Statistically processed data pertaining to amounts of free amino acids in the subjects' plasma are submitted in the form of tabulated material (see Table).

Free amino acids (mg%) in plasma of subjects while in a closed environment

Amino acid	Baseline period ($n=13$)	Day of study					After-effect period (6th d)
		no NH_3	with NH_3				
		6	6	13	25	37	
Isoleucine	0,53 ± 0,02	0,57 ± 0,04	0,62 ± 0,10	0,55 ± 0,05	0,54 ± 0,06	0,62 ± 0,06	0,60 ± 0,13
Leucine	1,11 ± 0,06	1,16 ± 0,05	1,20 ± 0,05	0,97 ± 0,13	0,93 ± 0,09	1,04 ± 0,15	1,17 ± 0,15
Valine	1,58 ± 0,11	1,92 ± 0,22	1,78 ± 0,12	1,91 ± 0,40	1,59 ± 0,02	1,67 ± 0,09	2,05 ± 0,24**
Threonine	1,95 ± 0,36	2,12 ± 0,13	1,83 ± 0,24	1,62 ± 0,25	1,26 ± 0,29	1,47 ± 0,20	1,11 ± 0,24**
Serine	0,93 ± 0,10	0,81 ± 0,06	0,97 ± 0,14	0,90 ± 0,12	0,81 ± 0,03	1,08 ± 0,05	0,99 ± 0,11
Methionine	0,21 ± 0,03	0,25 ± 0,03	0,24 ± 0,05	0,18 ± 0,03	0,22 ± 0,03	0,18 ± 0,02	0,26 ± 0,04
Tyrosine	0,55 ± 0,04	0,50 ± 0,07	0,56 ± 0,06	0,63 ± 0,11	0,60 ± 0,01	0,45 ± 0,05	0,83 ± 0,16
Phenylalanine	0,50 ± 0,04	0,46 ± 0,06	0,45 ± 0,11	0,58 ± 0,19	0,54 ± 0,05	0,47 ± 0,05	0,51 ± 0,08
Cystine ½	0,31 ± 0,04	0,25 ± 0,04	0,26 ± 0,09	0,20 ± 0,04	0,33 ± 0,02	0,24 ± 0,05	0,30 ± 0,05
Aspartic acid	0,21 ± 0,04	0,17 ± 0,03	0,17 ± 0,03	0,23 ± 0,02	0,16 ± 0,01	0,2[illegible] ± 0,03	0,21 ± 0,05
Glutamic acid	2,94 ± 0,34	2,95 ± 0,30	2,53 ± 0,30	2,45 ± 0,24	3,41 ± 0,52	4,04 ± 0,63*	4,58 ± 0,22*
Proline	1,63 ± 0,16	1,66 ± 0,14	1,55 ± 0,10	1,66 ± 0,20	1,31 ± 0,12	1,59 ± 0,06	1,97 ± 0,36
Glycine	0,95 ± 0,14	1,08 ± 0,13	1,11 ± 0,14	1,02 ± 0,13	1,07 ± 0,14	1,25 ± 0,19	1,10 ± 0,20
Alanine	1,93 ± 0,19	2,38 ± 0,22	2,37 ± 0,05	2,28 ± 0,26	1,93 ± 0,15	2,29 ± 0,09**	2,21 ± 0,34
Total	15,3	16,3	15,6	15,2	14,7	16,6	17,9

* $p<0.05$
** $p>0.05$

Results and Discussion

Assay of amino acid spectrum of subjects' plasma in the baseline period revealed a number of deviations from the physiological norm. Thus, we found lower levels of alanine, valine, proline and higher concentrations of glutamic and aspartic acids. The concentrations of these amino acids were either below the bottom of the normal range or somewhat above it [12]. The demonstrated changes can be attributed to the distinctions of the baseline period and concomitant nervous-emotional tension. As a rule, decline of plasma amino acid levels is observed under stress [2].

At the first stage of the period in the sealed chamber, there were no appreciable changes in plasma amino acid composition. Amino acid equilibrium persisted to the 37th day of the study. Starting on the 37th day, there was reliable increase in glutamic acid content and a tendency toward increase in alanine. There was also insignificant increase in total amino acid content (16.6 mg% versus 15.3 mg% in the baseline period). On the 6th day of the aftereffect period, blood amino acid pool increased to 17.9 mg% due to continuing increase in concentration of glutamic acid and tendency toward increase in plasma valine. An increase in the blood amino acid pool had also been observed in

the studies of N. S. Petrov [10] in subjects following a 10-day stay in a sealed chamber with high humidity. In the case of unchanged ambient parameters in the closed environment, the subjects presented, on the contrary, an insignificant decline of plasma amino acid levels [2].

The increase in glutamic acid concentration demonstrated in the present study is apparently not a chance finding. Amino acid metabolism proceeds in the body primarily via glutamic acid, as indicated by the data of Norberg et al. [16], who observed elevation of blood α-ketaglutaric acid. At the same time, it is known that amino groups of other amino acids are concentrated in glutamic acid. When there is a shortage of oxygen in the air (in this study, this probably did occur toward the end), amino acid metabolism increases [9]. It was also established that glutamic acid makes it possible to reduce significantly or eliminate entirely manifestations of hypoxia, which is associated with rapid elevation of initial oxygenation of blood [7]. The latter circumstance should have led to increased metabolization of glutamic acid followed by decrease in its concentration in blood. However, such a change did not occur. It is quite obvious that producing a specific atmosphere in the environment by continuously adding ammonia in a strictly graded concentration to the closed environment caused increased metabolization of ammonia due to its direct involvement in the transamination process, which in turn leads to decrease in activity of glutamic acid in the transamination process. This is why there was a decrease in utilization of plasma glutamic acid in subjects who were in an atmosphere containing ammonia, which ultimately affected its levels in plasma. Thus, the demonstrated increase in plasma glutamic acid concentration can be considered a natural response of the body to the higher concentrations of ammonia in the ambient atmosphere. The tendency toward increase in concentration of alanine demonstrated on the 37th day of the study can be considered to accompany accumulation of glutamic acid in blood, since alanine is also actively involved in transamination processes. In the presence of ammonia, the need for its involvement in this process must decrease. It should be noted that the aftereffect period, which lasted 6 days, was not long enough for normalization of amino acid equilibrium, and the glutamic acid level did not reach baseline values, while the concentration of blood alanine did revert to normal.

The results of this study of some aspects of human amino acid metabolism in a closed environment with high ammonia content in the atmosphere indicate that the body responds to this factor, which leads to decrease in metabolization of glutamic acid due to active involvement of ammonia in the transamination process. Moreover, the results warrant the belief that the data pertaining to plasma glutamic acid levels in man in sanitary-hygienic and toxicological studies of the air environment can be used as a test parameter for assessment of adaptive responses of man, and they can serve as an indirect parameter for evaluating toxicity of the environment.

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ANALYSIS OF WATER RECOVERED AFTER BEING USED FOR WASHING BY MEN AND WOMEN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 8 Dec 86) pp 53-57

[Article by A. A. Berlin and S. L. Chekanova]

[English abstract from source] The composition of wash water used by men and women was investigated. The results were exposed to multifactorial statistical analysis using the method of principal components. The investigations allowed the following conclusions to be made: 1) wash water used by men and women is comparable in composition; therefore the sex of the crewmembers of space vehicles can be disregarded when designing water reclamation systems; 2) three parameters, viz. oxidability, electric conductivity and chloride content, can be adequately used to assess the quality of utilized wash water; 3) the composition of wash water is largely dependent on the health status of its users.

[Text] Extension of spaceflight duration makes it necessary to develop onboard water supply systems based on reuse of wash water (WW). Determination of the composition of impure WW is important to development of the technology for its purification. This paper deals with one of these problems, i.e., comparative analysis of composition of impure WW recovered after its use for washing by men and women, as well as comparability of the water used by the two sexes. The importance of this matter is attributable to the future use of mixed crews in space missions. It is necessary to determine the composition and compare WW in order to solve the problem of method to be used for reclamation of impure WW. It can be assumed that the composition of impure WW depends primarily on the substances discharged by sweat and sebaceas glands on the skin surface, as well as residual amounts of waste and mechanical pollutants in the environment. Discharges related to the physiology of women may be of some significance. We know from the literature [1, 2], that one can consider the amount of sebum excreted is the same in men and women of the same age. Living under the same conditions and performing similar work, using underwear and clothing made of the same materials cause the same mechanical and bacterial contamination of the skin surface in men and women.

At the same time, it is known that women perspire considerably less than men. These sex-related differences are related to the milder response of female sweat glands to aetylcholine, which is the initiator of perspiration. However,

apocrine glands function more intensively before and during the menstrual period, which elicits increased perspiration and at this time it is comparable to perspiration in men. Thus far, the nature of other changes in condition of the integument and composition of discharge-contaminated WW related to this physiological process has not been studied. However, in this study we proceeded from the fact that these changes could not have an appreciable influence on overall quantitative characteristics of foul WW after use by men and women. We also took into consideration the use of cosmetics and perfumes that are used by women by virtue of the psychological stereotype and often due to an objective need. With these factors in mind, we examined the main physicochemical parameters of foul WW that are necessary for development of reclamation systems to supply water for hygienic purposes.

Methods

We matched a group of essentially healthy men and women 25 to 50 years of age (12 each) for this study. We analyzed foul WW after each of the subjects took a shower. They showered once every 7 days. The participants were allowed, if necessary to wash their face and hands daily. The amount of water used for the showers and soap was strictly dosed. For more precise determination of composition of foul WW, distilled water was used for the showers. We determined the following physicochemical and microbiological parameters of the foul WW: biochromate oxidation, electric conductivity, hardness, odor, transparency, amount of soap, chlorides, ammonia, total microbial bodies per milliliter used WW. The temperature of shower water was 43±2°C.

It should be noted that the women who participated in these studies were not limited with respect to use of their usual perfumes and cosmetics. They used lipstick, perfume, cream, powder, deodorants (both domestic and imported), etc. All of the studies were conducted in a special shower compartment which permitted complete collection of used WW into a container individually from each shower, and from it an averaged sample was taken for analysis. It was necessary to have averaged water samples because the first and last batch of wash water contained different amounts of pollutants. The individuals involved in the experiment underwent a medical examination before and after taking the shower: we measured arterial pressure (BP), body temperature, pulse rate and a number of other parameters.

The obtained data were submitted to multidimensional statistical analysis using the method of principal components (MPC). This method enables us to obtain from the baseline tags the principal components (PC), which are linear combinations of baseline data. The PC can be considered integral parameters according to which one can, for example, classify objects. PC are the endogenous characteristics of an object, and one can estimate the coefficients of correlation between them and parameters, as well as their contribution to overall dispersion (factor structure). The calculations were made on a YeS-1033 computer using standard programs [3] for the informative parameters singled out in the program: oxidizability--COM [chemical oxygen minimum], chloride content, conductivity. To assess the reliability of differences between the two groups of generalized parameters we used a frequency criterion [4] of the following appearance:

$$Z = \left(\frac{M_1}{N_1} - \frac{M_2}{N_2}\right) \times$$

$$\times \Big/ \sqrt{p^*(1-p^*)\left(\frac{1}{N_1} + \frac{1}{N_2}\right)},$$

where $p^* = \frac{M_1 + M_2}{N_1 + N_2}$,

M_1 and M_2 are number of men and women, respectively, for whom the parameter is less than or equals 2; N_1 and N_2 are sample sizes (number of experiments).

More than 500 showers were taken in the course of the studies.

Results and Discussion

Table 1 lists the results of analyses indicating that WW recovered from men and women has similar values for parameters, i.e., its composition is comparable. We paid attention to the fact that there was change in parameters of WW recovered from the same subjects as a function of their health status. Table 2 lists data obtained from the showers with consideration of this factor. The first column subject numbers, the Status column lists data obtained after the showers were taken by subjects with colds and viral diseases and elevated BP. Mean values for the analyzed parameters of WW recovered from the same subjects in a healthy condition were taken as the norm. Interestingly, maximum changes in function of the integument and, consequently, in composition of WW were observed in the presence of cardiovascular disease rather than colds and viral diseases.

Table 1. Mean and standard deviations of parameters of WW composition

Group	COM (mg O_2/ℓ)		Conductivity (Ω/cm)		Chlorides (mg/ℓ)	
	M	σ	M	σ	M	σ
Men	1565	315	$1,63 \cdot 10^{-4}$	$0,83 \cdot 10^{-4}$	20,54	9,49
Women	1431	312	$3,17 \cdot 10^{-4}$	$1,16 \cdot 10^{-4}$	39,14	11,35

The results of these studies demonstrated the validity of our hypotheses to the effect that the parameters of WW recovered from women depend little on menses. It was established that there is a 10-20% rise in parameters on the first and last day of the menstrual cycle, provided BP, pulse and temperature are normal. However, as can be seen in Table 1, these one-time rises do not affect the mean values.

Another important finding of the study was determination of the comparative informative value of the different parameters of WW considered. Three parameters, which are described by two PC of the aggregate of data in question, were found, one of which characterizes sebum discharge and the other, the excretion from sweat glands. Thus, only two of the entire set of factors affecting the nature of contamination of the integument were found to be significant,

Table 2. Correlation between physiological condition and principal physicochemical parameters of WW [ARD--acute respiratory disease]

Subject No	Health status	COM (mg O_2/ℓ)	Conductivity (Ω/cm)	Chlorides (mg/ℓ)
1	ARD	1600	$1{,}8\cdot10^{-4}$	19,88
	Norm	1230	$1{,}9\cdot10^{-4}$	18,7
4	ARD	1800	$1{,}12\cdot10^{-4}$	21,3
	Norm	1340	$1{,}4\cdot10^{-4}$	19,2
8	BP 180/110	2300	$6{,}0\cdot10^{-4}$	79,52
	Norm	1200	$4{,}0\cdot10^{-4}$	17,0
11	BP 160/100	2000	$1{,}58\cdot10^{-4}$	15,62
	Norm	1400	$2{,}34\cdot10^{-4}$	9,47
12	BP 160/110	2100	$1{,}06\cdot10^{-4}$	9,94
	Norm	1350	$1{,}45\cdot10^{-4}$	10,8

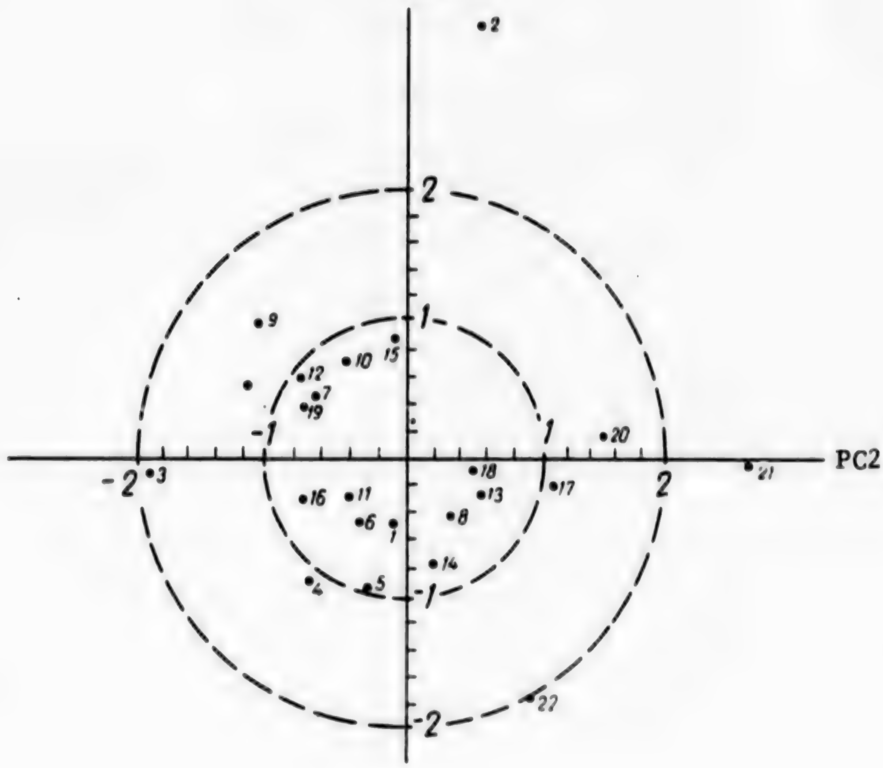
Table 3. Factor structure of results of estimating composition of WW

PC	Weight factors between components and parameters					
	Men			Women		
	COM	conductiv.	chlorides	COM	conduct.	chlorides
First	−0,03	0,89	0,89	0,6	0,81	0,84
Second	0,99	0,88	−0,04	0,8	−0,37	−0,21

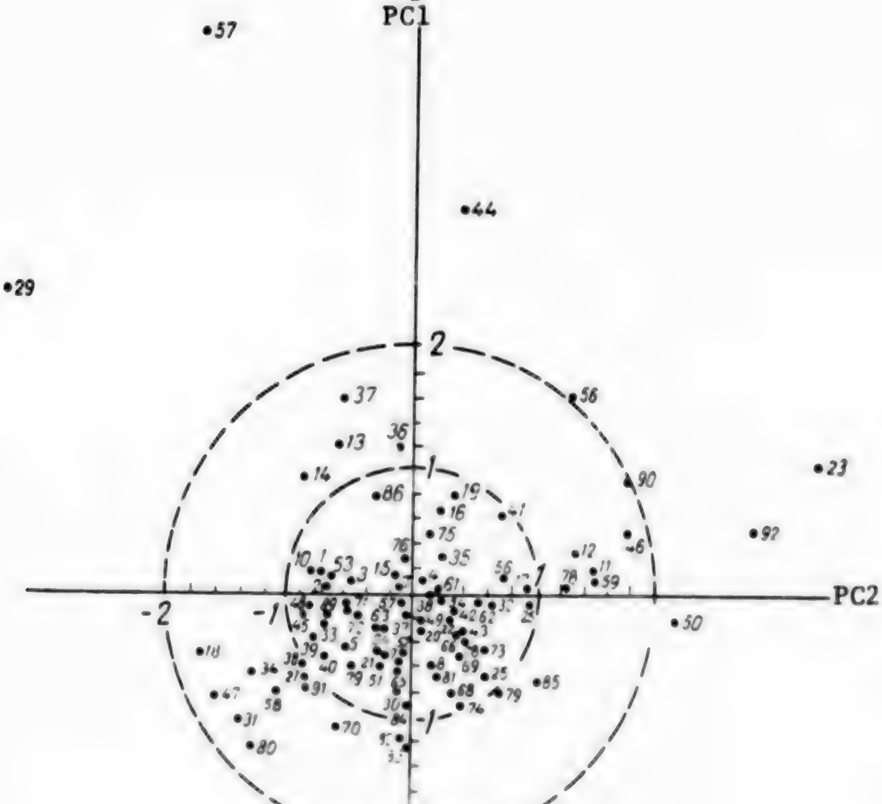
and they were unrelated to sex. Their influence was described, virtually entirely, by parameters of conductivity, chloride content, as well as COM, which makes the greatest contribution to overall dispersion (factor structure). The other physicochemical and microbiological parameters of WW were approximately stable, and for this reason were not informative. The relevant data are submitted in Table 3. It was found that PC1 is correlated the most closely with conductivity and chloride content, which reflects perspiration function, while PC2 has a high coefficient of correlation with COM (i.e., presence of organic impurities) of WW, which characterizes mainly the function of sebaceous glands. It should be noted that the factor structure is the same for men and women. The results are encouraging, since these 2 components descirbe 85% of the scatter of baseline information. However, we were impressed by the fact that the parameters of conductivity and chloride content showed a rather distinct correlation to sex, while COM of WW did so to health status. The latter parameter, which shows virtually no response to sex, demonstrates stable and significant changes in this case and is a function of nature of disease (see Tables 1 and 2).

The Figure is a graphic illustration of generalized parameters characterizing the condition of wash water from showers in the space of PC1 and PC2. As can be seen in this figure, all points are essentially contained within a circle the radius of PC value of which is 2. All results obtained on absolutely

a



b



healthy subjects are contained in a circle with radius 1. There are points between the boundaries of circles with radii 1 and 2 that describe data obtained from subjects in an essentially healthy condition but with insignificant deviations from their usual norm (menstrual period, condition preceding and following an illness). The points beyond the circle correspond to WW recovered from people with some physiological deviation (elevated BP, acute respiratory disease) at the time of showering. We were impressed by the fact that there was total coincidence of data obtained graphically and listed in Table 2.

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CLINICAL STUDIES

UDC: 616.1-057-037:613.693

FORECASTING COMPLICATIONS OF CARDIOVASCULAR DISEASE IN FLIGHT PERSONNEL

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 30 Jan 87) pp 57-62

[Article by G. L. Strongin, A. S. Turetskaya, B. L. Gelman and O. N. Rodionov]

[English abstract from source] The flying personnel of different age groups, including those who continued their professional activity and those who were grounded because of cardiovascular diseases, were followed up for a long period of time. The prognostic value, sensitivity, specificity of various risk factors, symptoms and syndromes of cardiovascular diseases were investigated. Using mathematical prediction methods (Wald's sequential nonhomogeneous statistical test), a diagnostic table for predicting outcomes of cardiovascular diseases for the immediate 5 years was developed. The table was checked and tested on a control sample. The trial showed that the table provided a bettery accuracy of prediction than the traditional methods normally used in the expertise practice.

[Text] One of the most important parts of expert medical certification of flight personnel (EMCF) in civil aviation (CA) is diagnostication and expert evaluation of diseases of the cardiovascular system, since such diseases present the main threat to flight safety, and they are the most frequent cause of medical disqualification [6, 8, 15].

Clinical, roentgenological, biochemical, electrocardiographic methods and functional tests (primarily physical loads, hypoxic tests) are used for the detection of early and discrete forms of cardiovascular pathology in flight personnel [5, 6, 9]. The increase in scope of work-up and large number of diagnostic signs obtained result in an increase in share of individuals with deviations of some parameters or other from the norm. The boundaries between healthy and sick people are growing more and more obscure; the clinical signs of nosological forms are growing less typical. A large category of individuals has appeared among flight personnel that are referable to the risk group for onset of ischemic heart disease (IHD).

Under existing conditions, prognosis of cardiovascular disease based on clinical and empirical experience of expert physicians is growing increasingly difficult, since the personal experience of each physician comprises only isolated

cases of adverse outcome of disease. At the same time, prolonged epidemiological methods of studying cardiovascular pathology have led to development of a mathematical system for predicing the possibility of development of sudden death, myocardial infarction, cerebrovascular accident and other complications of diseases [1, 10, 11, 12, 13]. With such an approach, it is not formulation of a diagnosis but consideration of the presence and severity of prognostically relevant signs that becomes crucial to a prognosis.

Several difficulties are encountered when making direct use for EMCF of prediction models developed for epidemiological studies, which are related both to the scope and methods of examination, as well as distinctions with respect to the attitude of flight personnel toward examinations. In view of their high motivation to continue flying, flight personnel often distort answers when standard questionnaires are used, there have been instances of taking drugs prior to a routine certification (particularly in the presence of hypertension). The distinctions of flight work lead to changes in lipid metabolism that distinguish the pilot population from analogouspopulations of healthy males [3, 7]. If we also consider that the prognostic value of different signs varies markedly when testing different populations in diffferent countries [1, 11, 14], it becomes obvious that without a lengthy verification (actually without conducting a second examination), it is impossible to use the existing models to make expert decisions.

Our objective here was to elaborate a prognostic rule for CA flight personnel on the basis of long-term clinical observation of both individuals who continue to fly and those who have stopped flying.

Methods

We analyzed the data obtained from 636 clinical examinations of 292 people over a 20-year follow-up period, which were performed by us.

At the start of the study, there were 91 people with the diagnosis of "healthy" (average age 39±6 years); atherosclerotic pathology of the aorta and heart were found in 116 people (average age 48±6 years) and neurocirculatory dystonia of the cardiac type (NCD) was found in 85 (average age 36±5 years).

Vital statistics, history, physical, roentgenological, biochemical, electrocardiographic and functional diagnostic data obtained in the first examination made up 42 tags.

Clinical and prior history data were entered in accordance with a form adopted in EMCF, and instrument tests were performed using standard methods.

The entire sample was divided into groups with favorable and unfavorable outcome, according to course of illness. The unfavorable outcome group referred to clinically marked forms of cardiovascuar pathology presenting a severe threat to flight safety: suddent death, myocardial infarction, angina, cerebrovascular accident. Medical documentation with description of the acute period of disease and appropriate ECG [electrocardiogram] dynamics served as grounds for diagnosing prior myocardial infarction: appearance of changes on the ECG corresponding to Minnesota code 1-1, 1-2 without the typical pain syndrome. Cases of typical complaints (pain under the sternum or in the

left chest arising upon walking and disappearing within 10 min after stopping) were taken as angina. Presence of "possible" ischemic changes on the ECG (classes 4.1, 5.1 without 3.1) without other clinical manifestations were not considered an adverse outcome.

When processing the data on a computer, we calculated the relative risk for different tags, determined sensitivity, specificity and prognostic value of the tags using the method in [4].

The prognostic table was plotted on the basis of a sequential heterogeneous statistical procedure described in [2]. We selected this algorithm for the following reasons: in the first place, this procedure is convenient for the clinical physician and does not require use of computers; in the second place, it is already in use in the CA for purposes of occupational psychological screening; in the third place, it will make it possible to add new informative tags to the diagnostic table in the future without altering old ones (after checking their correlation with old tags). The latter is the principal point, since addition of new methods and upgrading of old ones should not change entirely the whole prognostication algorithm.

Results and Discussion

In the observation period, the incidence of complications of cardiovascular pathology (adverse outcome) constituted 14%, including the following: sudden death (7%), myocardial infarction (38%), stress angina (48%) and cerebrovascular accident (7%). Of the total number of complications, 43% arose in the first 5 years of follow-up.

An adverse outcome developed in 3.4% of the individuals deemed to be healthy when submitted to medical certification, 10% of those with the diagnosis of NCD and 26% of those with the diagnosis of atherosclerosis of the aorta and coronary arteries. The course was particularly unfavorable in the case of atherosclerosis detected at up to 40 years of age (the incidence of complications was 12 times higher than for healthy individuals and 4.3 times higher than for NCD at the same age).

The incidence of complications was substantially higher among those who had been grounded than those allowed to continue flying. In 5 years, this parameter constituted 30 and 5%, respectively, in 10 years--70 and 15%. It was found that the expert approaches used in the CA have 50% sensitivity, 83% specificity and only 7% prognostic value in the case of predicting adverse outcomes for the next year, the figures for a 5-year forecast being 43, 96 and 30%, respectively. Forecasting for a longer term leads to considerable decline of sensitivity and is virtually inexpedient. At the present time, EMCF provides for reduction to one-half in incidence of acute complications of cardiovascular diseases among flight personnel.

The obtained data enabled us to make a quantitative evaluation of the significance of different risk factors, symptoms and syndromes to prediction of complications of cardiovascular disease in flight personnel.

Diagnostic table for predicting outcome of cardiovascular diseases among CA flight personnel (over 5-year period)

No	Tag (symptom)	DC
1	Resting ECG:	
	ischemic depression of ST segment	+104
	inversion of T wave	+37
	depression of T wave	+1
	ischemic depression of ST segment or inversion of T during positive orthostatic test or under normalizing effect of β-blocking agents	+10
	no ECG changes	-16*
2	Exercise ECG:	
	ischemic depression of ST segment during double Master's test or 500 kg-m/min (80 W) on cycle ergometer	+82
	ischemic depression of ST segment at submaximum exercise on cycle ergometer	+64
	ischemic depression of ST that is not reproducible after intake of β-blocking agents	+10
	no ischemic depression of ST during exercise	-59
3	Syndrome of enlargement of left ventricle:	
	combination of roentgenological and ECG tags	+117
	roentgenological enlargement of left ventricle	+80
	left ventricular hypertrophy on ECG (according to Sokolov-Aayon criteria)	+70
	no enlargement of the heart	-45
4	Syndrome of physical changes in the heart (percussive dilatation of heart margins to the left, dull sounds):	
	present	+49
	absent	-94
5	Heredity: unfavorable	+39
	favorable	-11
6	Diastolic BP at submaximum exercise on ergometer:	
	no more than [sic] or equal to 100 mm Hg	+52
	less than 100 mm Hg	-23
7	Resting diastolic BP: higher than or equal to 90 mm Hg	+31
	less than 90 mm Hg	-11
8	β-Lipoproteins: over 800 mg%	+30
	equal to or less than 800 mg	-8
9	Blood serum choleterol: over 260 mg%	+22
	equal to or less than 260 mg%	-16
10	Smoking: smoker	+21
	nonsmoker	-29
11	Exercise: none, irregular	+11
	regular	-59

Note: A plus sign is indicative of probability of adverse outcome, minus sign, of a favorable outcome.

Symptoms and risk factors are divided into three groups according to their prognostic properties. The first group includes symptoms with relatively high prognostic value (54%) and specificity (98%), but low sensitivity (23%):

ischemic depression of ST segment at rest and during double Master's test. The presence of these symptoms is indicative with high reliability of the possibility of adverse outcome, but their absence is not of great significance to predicting a favorable course of disease; the second group refers to symptoms with adequate prognostic value (25-31%), sensitivity (31-52%) and specificity (76-87%): ischemic depression of ST segment during submaximum exercise on ergometer, elevation of diastobic arterial pressure (BP) during such exercise to more than 100 mm Hg, hypertrophy of left ventricle according to roentgenological and ECG tests, adverse heredity. These parameters make a substantial contribution to prediction of both unfavorable and favorable outcome; the third group refers to symptoms with high sensitivity (56-83%) but low, although reliable, prognostic value (19-21%) and specificity (36-62%): nonspecific changes in ST segment and T waves at rest, dilatation of heart margins to the left, dull sounds, increase in β-lipoproteins of blood (over 800 mg%), increase in body weight index (over 30), smoking, no regular exercise. These symptoms are widespread among flight personnel with both favorable and unfavorable outcome. They are of ancillary relevance to prognostication.

Data were obtained to the effect that such an important and well-known symptom as elevation of BP has low informativeness in prediction of adverse outcome among flight personnel. At the same time, signs indirectly related to essential hypertension were highly informative: roentgenological enlargement of the left ventricle, nypertrophy of the left ventricle according to ECG data. There are grounds to believe that flight personnel with elevated BP take hypotensive agents when undergoing medical certification. Irregular self-treatment of essential hypertension does not prevent myocardial hypertrophy or complications related to this pathology. Hypertrophy of the left ventricle was found in 37% of the pilots undergoing echocardiographic examination and referred for a work-up in the hospital with normal BP [9]. Latent hypertensive reactions were also found during the cycle ergometer tests, as a result of which, such a tag as elevation of diastolic BP (over 100 mm Hg) acquires greater diagnostic value than resting BP.

It should be noted that the list of prognostically significant signs included some that are rarely examined in epidemiological studies because they have not been standardized well, but nevertheless they are used extensively in EMCF practice. We refer to the physical changes in the heart and its enlargement. A great responsibility is placed upon specialists with regard to determining these parameters and standardizing methods, for example, use of roentgenocardiometry.

Long-term follow-up made it possible to evaluate in a different aspect the significance of the hypersympathetic ECG syndrome, which is the basis of the diagnosis of NCD of the cardiac type. It confirmed the previously validated view, which is adopted in EMCF, that there is a more favorable outcome of this pathology than atheroclserotic involvement of the heart with analogous ECG changes at rest and during exercise [6].

The prognostic value of changes in the end part of the ventricular complex on the ECG, which build up during the orthostatic test and disappear or diminish considerably after intake of β-adrenoblockers, constituted 13%, which is reliably lower than the prognostic value of analogous, but persistent ECG changes--35%. It is important to mention that it is still reliably higher

than with a normal ECG (3%). It has been established that cardiovascular disease complications developed at over 45 years of age in the group with NCD. In most cases, there was change in the clinical appearance of disease 1-2 years prior to development of an adverse outcome: lability of ECG disappeared, there was disappearance or dramatic decrease in normalizing effect of β-adreno-blockers, signs of left ventricular hypertrophy appeared. Complications of IHD developed without prior changes in nature of illness in only 2 out of 8 cases.

On the basis of a study of the informativeness of different tags and their correlation, a diagnostic table was elaborated for predicting the outcome of cardiovascular disease among flight personnel. The table listed tags with reciprocal correlations of no more than 0.2, and for this reason it did not include such a significant tag as age, which is correlated on a higher level with a number of tags. The need to provide high flight safety was taken into consideration in selecting diagnostic thresholds, which it is suggested to set at 80 and 95% of the reliability level (sum of diagnostic coefficients over +90 and less than -130). The method of working with the table is as follows: the obtained diagnostic coefficients (DC) are added successively with consideration of sign. If the subject has several symptoms combined in one tag, the one with the highest DC is taken. The only exception is ischemic depression of ST or inversion of T at rest and during exercise, which is not reproducible after intake of β-blockers. For such individuals, DC equals +10, rather than +104 or +64. When necessary, a combination of two symptoms is considered (for example, item 3 in the table). Addition is stopped when the sum reaches or exceeds +90, or else when it drops to -130 or more. Further addition does not improve prognostication, since it is based on less reliable tags. For individuals whose DC equals +90 or more, development of complications of cardiovascular disease within the next 5 years is predictable at 80% reliability. A sum of -130 or less (i.e., -140, etc.) permits prediction at 95% reliability that complications of a cardiovascular disease will not occur within this period. If the sum does not reach +90 or -130 after adding all DC's, the prognosis remains uncertain.

We checked the accuracy of forecasting with use of the diagnostic table on a control sample of 106 people with known outcome of disease, and compared it to EMCF conclusions. An adverse outcome developed in 37 out of the 106 subjects. Such a prognosis was made by the EMCF in 16 cases (43%). It was predicted for 28 people (76%) with use of the table, it was uncertain in 6 cases and favorable in 3. Among individuals for whom the EMCF conclusion was that they were fit for flight work, 22% developed complications of disease, as opposed to 6% of those with favorable prognosis with use of the table.

Thus, long-term observation of health status of flight personnel made it possible to determine the probabile significance of different risk factors and symptoms, and to suggest more formalized approaches to forecasting acute complications of cardiovascular diseases.

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EVALUATION OF 'SPARE ROOM' IN CEREBROSPINAL SYSTEM USING NONINVASIVE METHODS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 27 Feb 87) pp 62-65

[Article by L. G. Simonov, A. K. Tsaturyan, A. S. Saribekyan and L. G. Shmidt]

[English abstract from source] This paper presents a theory according to which fluid volumes and pressures in the cerebrospinal system should be related nonlinearly rather than exponentially. The curve describing elasticity E as a function of pressure P should have two almost linear segments separated by an intercept. This concept is based on experimental and model data suggesting that the cerebrospinal system can be viewed as an elastic cavity which can, at normal and low pressures, trap an additional volume of any CSF component and shift other components; as a result, this leads to a linear increase in pressure within the cavity. The theoretical concepts found support in comparative invasive-noninvasive studies of the intracranial fluid with the aid of ultrasonic introscopy and in postural tests to which patients with cerebral lesions were exposed. A noninvasive technique for measuring fluid volumes and pressures in the cerebrospinal cavity was developed. The technique can be used as a diagnostic tool in the case of intracranial distension.

[Text] When studying biophysical and physiological patterns of intracranial dynamics of cerebrospinal fluid (CSF), analysis of relationship between volume V and pressure P in the cerebrospinal system has clinical diagnostic and prognostic significance [3, 4, 6, 8, 9].

Data obtained from research and diagnostic procedures on patients with brain lesions [1, 7] made it possible to develop the conception of so-called "spare room" in the cerebrospinal system and expound the hypothesis that it could be defined by noninvasive methods [7]. We discuss here the possibility of estimating the "spare room" according to results of ultrasonic echoencephaloplethysmography with use of change in body position for graded change in intracranial pressure.

Methods

We examined 15 neurosurgical patients with impaired cerebral circulation and cerebrocranial trauma, as well as 30 healthy subjects. We took intracranial pressure on six patients using a ventricular drain or subdural balloon inserted for therapeutic purposes. The neurosurgical patients and healthy subjects were submitted to echoencephaloplethysmography (EEP) [5]. We used a fronto-occipital lead for an ultrasonic signal from the occipital bone, changes in which (U_{es}) are due to volumetric changes in the lateral cerebral ventricle [4]. The subjects were placed on an electrically driven orthostatic table, which enabled us to move their head and trunk continuously (at the rate of 1°/s) in relation to the horizontal plane within the range of angles β = ±15°. The patients were moved to angles β not exceeding -6°.

All moves were made in relation to the axis of the orthostatic table which coincided with the end of the lumbar canal as verified by the location of the iliac bone.

The obtained data were processed on an Iskra-1256 microcomputer, and they were also approximated with spline functions using a program run on an SM-4 computer.

Results and Discussion

The invasive examination of intracranial pressure (P) of neurosurgical patients during the postural test revealed, as was to be expected, that pressure increment (ΔP) was a linear function of change in angle of the body ($\beta°$), and this function is expressed by a regression equation:

$$\Delta P = 6.8\beta + 6.78 \qquad (1)$$

with coefficient of correlation r = 0.93. Apparently the length of the lumbar canal can affect function $\Delta P = f(\beta)$. In addition, the value of ΔP can be affected by the response of central and intracranial hemodynamics of a vascular nature, which arises with change in body position in relation to the horizontal plane. Figure 1 illustrates the "corridor" of ΔP values, which are limited by the lines of regression for lumbar canals 500 and 700 mm in length (which correspond to heights of 140 to 170 cm for an individual). The values for ΔP obtained with equation (1) are situated mainly within this corridor. This confirms the hydrostatic nature of changes observed during postural tests.

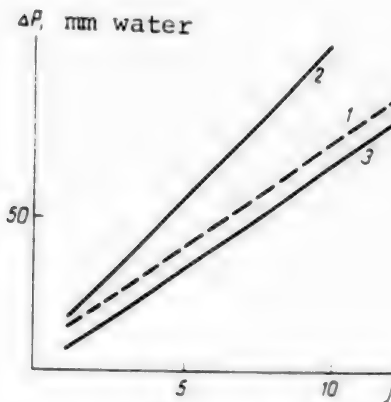

Figure 1.
Pressure (P) in cerebrospinal system as a function of turntable angle ($\beta°$) for entire sample of cases (1) with relatively short (3) and long (2) cerebrospinal canal
Explained in the text

During postural tests on neurosurgical patients, a direct method was used to demonstrate changes in intracranial (cerebrospinal fluid) pressure ΔP, and non-invasive methods were used to determine volume ΔV (i.e., U_{es}). A nonlinear

function was obtained, which was approximated with a spline function (Figure 2a and b). By referring pressure increment ΔP to increment in level of echo signal ΔU_{es}, we obtain modulus of elasticity $E = dP/dU_{es}$. Analysis of changes in E with growth of P (Figure 3a) reveals 2 segments of the curve, horizontal and sloped, with a point of inflexion in the region of P = 195 mm water.

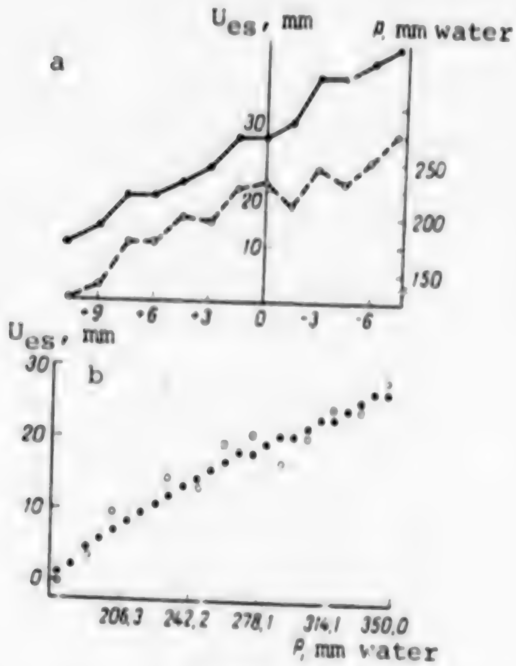

Figure 2.
Changes in pressure P and volume parameter U_{es} with body moves in relation to horizontal plane (a) and relationship between these parameters (b)

a) dots show pressure (P), circles are volume parameters (U_{es})
b) ○-baseline data for relationship between pressure P and U_{es}; ●--values for spline function

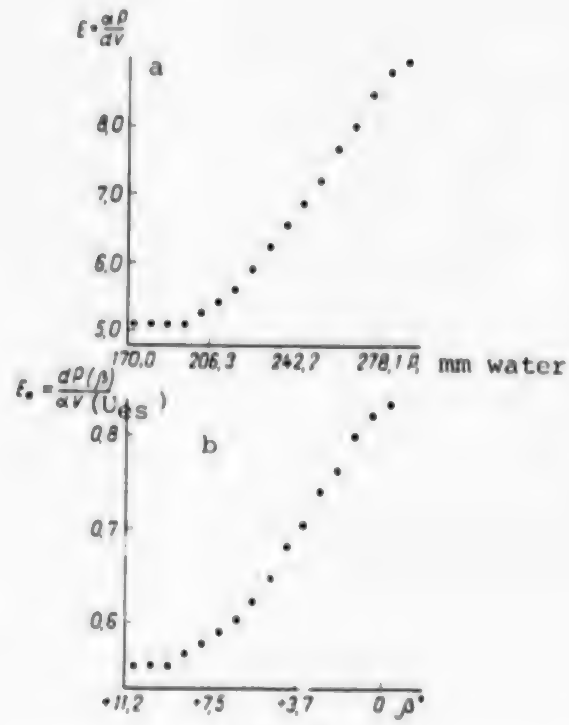

Figure 3.
Invasive-noninvasive characteristics of function $E = f(P)$ (a) and noninvasive characteristics of $E = f(\beta)$ (b)

Considering P as a function of angles of body inclination, one can use $\beta°$ instead of P to estimate E. Then, expression E will contain only values obtained by noninvasive methods, $E_* = dP/dU_{es}$. E_* as a function of $\beta°$ is illustrated in Figure 3b. Apparently, the point of inflexion of function $E_* = f(\beta)$ corresponds in pressure to the point of inflection of function $E = f(P)$.

Having thus obtained characteristic P-V of the function and a theoretical idea about the mechanism of its formation, we can assess the nature of intracranial dynamics of cerebrospinal fluid.

Thus, the presence of a linear relationship between change in position of the body and increase in intracranial pressure enables us to use the postural test for graded change in pressure P in the cranial cavity. The fact that it is also possible to determine the nature of volumetric changes in the lateral

ventricle of the brain enables us to use a noninvasive method to obtain a P-V type function which provides diagnostically significant information about the intracranial volumetric correlations between fluids. The segment of the curve in which E_* does not increase with change in β or increases insignificantly is characterized by the presence of "spare room" in the cerebrospinal system, and it is defined as the "region of optimum pressure" [7].

The point of inflexion of the curve corresponds to maximum area of optimum pressure. The area of pressure P where there is increase in elasticity E_* is characterized by decrease in "spare room" in the cerebrospinal system [7, 10].

If we consider the known normal range [7] for cerebrospinal pressure (70-200 mm water) within which there is "spare room," it becomes obvious that presence of a horizontal section E in the region of 0°, as well as its maximum value with small (up to $\beta° = -10 \div -15°$) negative angles is indicative of absence of hypertension. This segment and point of maximum optimum pressure region are in the area of positive angles, which means that the spare room has been exhausted in horizontal position. According to Figure 3b, maximum value for the region of optimum pressure corresponds to angle $\beta \approx +10°$ or cerebrospinal pressure P = 195 mm water. It is obvious from Figure 2 that the horizontal position of the subject corresponds to hypertension in the cerebrospinal system.

When testing healthy subjects and patients without signs of hypertension, the maximum value for the horizontal segment of curve E was usually in the range of negative angles of body inclination.

The above-described noninvasive approach, which involves the combined use of ultrasonic echolocation and postural test, can be used to determine intracranial pressure of patients with conservative management and, perhaps, healthy people.

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METHODS

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ISOTOPE METHODS OF DETERMINING DISTRIBUTION AND MOVEMENT OF BLOOD IN THE BODY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 17 Feb 87) pp 65-67

[Article by V. I. Lobachik, V. N. Korsunskiy, V. I. Popov, S. V. Abrosimov, V. V. Zhidkov and V. A. Andretsov]

[Text] Migration of blood into the capacitive vessels of the upper half of the body is one of the vivid manifestations of the effect of weightlessness on man [1-4, 8].

Basic research on the phenomenon of redistribution of blood during spaceflights is difficult at the present time. For this reason, researchers are trying to solve a number of problems through ground-based model experiments with antiorthostatic hypokinesia, which makes it possible to produce gravity redistribution of blood in the body over a wide range. However, the extent of redistribution of blood that should be reproduced in such experiments is not known. In such a situation, it is probably expedient to search for general patterns in the response of the circulatory system to plethora of the vascular collector of the upper half of the body. It is quite apparent that, in all cases, the researcher must make a strict quantitative evaluation of the process of redistribution and shifting of blood in the human body and its different regions. The possibility has been explored of using for this purpose methodological procedures such as plethysmography, rheography, thermography, etc. [3, 6]. However, these methods can provide only a qualitative assessment of the process in question.

In our opinion, radiotracer methods could make some contribution to solving this problem. They are physiological and can record, with high degree of precision and adequate reliability, rapid processes in the body. We analyzed the capabilities, advantages and drawbacks of such methods. We studied and tested different methodological approaches and apparatus, which enabled us to formulate a list of general requirements and conditions imposed upon such a method: the method must provide a strict quantitative evaluation of the process of distribution of blood in the body and record, with a high degree of precision and reliability, all of its shifts both in the body as a whole and its different regions; the method must be universal and consider the entire diversity of ground-based experiments with hypokinesia and immersion, i.e., the main models adopted in space medicine; the method should record and make

quantitative estimates of shifting of blood during such traditional tests in space physiology as the orthostatic test, test with lower body negative pressure (LBNP), cycle ergometry and others capable of causing redistribution of blood in the body. These are basic conditions, since there is a powerful compensatory apparatus for function of the circulatory system, and to diagnose its state it is necessary to use additional load tests.

When defining special radiological requirements for the method under discussion, one should single out the following which are the most important: choice of isotope, conditions of taking radiometric measurements and instrumentation. Since we are dealing with the question of studying circulatory function of the body, it is quite apparent that the isotope must be introduced into blood, it should be uniformly distributed in it and provide information about its distribution and shifting through its emission. Hence, some specific and rather rigid requirements are imposed on the choice of radioactive tracer.

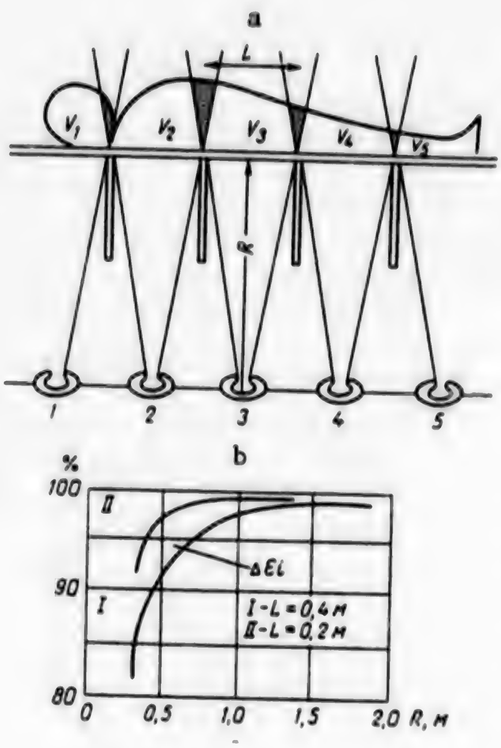
Since blood is a complex biological tissue, either plasma or a red blood cell may be the carrier for the isotope. Use of an isotope alone will not fully reflect the condition and nature of circulation, since we know that the amounts of these parts of blood can change to varying degrees under the conditions of model experiments, as well as under the effect of functional tests. Consequently, to solve these problems it is desirable to pursue concurrent studies of kinetics of both blood plasma and its erythrocyte pool.

Thus, when choosing two radiotracers, each of them should meet the following specifications: it must not seek any single organ or tissue; it must be a γ-emitter; it must have a solid bond with the carrier and remain in the blood stream for a rather long time, and it must not become involved in metabolic processes; it must have a short half-life; there must be a minimal radiation burden; when two isotopes are used simultaneously, their energy must be different and well-discriminated.

Of the entire current armamentarium of radiopharmaceutical agents, the possibility of choice turned out to be quite limited. As a rule, the following nuclides are used to label plasma: ^{131}I-albumin, ^{99m}Tc-albumin, ^{113m}In-citrate. For red blood cells, ^{51}Cr, ^{59}Fe-citrate or ^{99m}Tc-pyrophosphate are generally used.

A number of isotopes were found to be unsuitable or inappropriate for the goals set forth. This category includes ^{131}I-albumin, which is traditionally used to measure plasma volume. Its energy composition is heterogeneous. The yield of γ-radiation from this isotope is only 9%, for which reason unjustifiably large doses would have been required for the tests. The other radionuclides mentioned, ^{99m}Tc-albumin and ^{113m}In-citrate, are steady γ-emitters with short half-life and are entirely suitable for the above-mentioned studies.

In our opinion, ^{51}Cr is unsuitable for labeling red blood cells. The method of labeling erythrocytes is traumatic and elicits hemolysis. In addition, chromium is toxic to red blood cells. In our opinion, ^{59}Fe is also unsuitable. It has the following flaws:



Radiometric set-up
a) diagram of location of sensors and shields
1-5) drawing of sensors
b) effectiveness of sensor reading as a function of linear size of tested region to the patient's body
Y-axis, $\varepsilon i = \varepsilon Vi/\varepsilon_0$ (%)

It is actively involved in complex metabolic processes of erythropoietic function of bone marrow and organs of the reticulo-endothelial system.

It can be used, to some extent, after maturation of erythrocytes in bone marrow and their discharge into the blood stream; however, this process is rather variable and, moreover, it can be reutilized.

Use of this isotope in model experiments is inexpedient, since erythropoietic function is subject to changes under such conditions.

The high energy of this isotope produces significant radiation burdens to the spleen and red marrow.

The permissible dose for tests must not exceed 0.2 MBq, which makes it difficult to record ^{59}Fe in low-background chambers and diminishes its effectiveness and reliability.

This isotope has a long half-life (44.5 days), which limits appreciably its use for dynamic observations.

Use of ^{99m}Tc together with pyrophosphate is considered optimum for our purposes. However, when using this radionuclide one must bear in mind the injected dose and radiation burden to the spleen.

Thus, of the above list of radionuclides, the optimum ones for our purposes are generator isotopes, ^{113m}In and ^{99m}Tc. Only ^{113m}In-citrate and ^{99m}Tc-pyrophosphate are suitable for concurrent tagging of plasma and erythrocytes.

Other extremely important conditions for isotope studies are: conditions of radiometric readings, which are also basic; the entire human body and its different regions of interest to the researcher must be within the field of the radiometry set-up, while the sum of activity of different regions should constitute overall activity of the body; the difference in reading activity from frontal and dorsal points of the human body must be reduced to a minimum.

It is apparent from these conditions that a multisensor system can serve as such a radiometric device. Analysis of the feasibility of using the existing assortment of radiometry instruments has shown that none can fully meet the above requirements and conditions. Thus, use of a total body counter precludes recording the process of migration of blood. Scanning of the entire body is suitable only for obtaining static characteristics of the process of

distribution of blood in the body, and it does not permit recoridng blood migration processes. For the same reason, the method of uniform movement of the subject under the sensory or other radiometry system is also unsuitable. In spite of the obvious advantages and vast diagnostic capabilities of modern gamma chambers, they too cannot solve the problems in question entirely. Consequently, there must be a different radiometry set-up that meets all of the above requirements and can perform the formulated tasks.

Such a special radiometry set-up was developed and awarded an author's certificate [5]. It consists of a multisensory system for concurrent recording of both the activity of the entire body and of its different regions--head, chest, abdomen and lower extremities (see Figure). Scintillation sensors are situated underneath each region (two sensors under the lower limbs). Lead shields are placed between these regions and they virtually preclude registration of activity from adjacent regions. Such a multisensor system with several shields permits concurrent recording of activity in each region separately and in the body as a whole; thus, the process of movement of blood in them can be monitored. Several conditions must be met for such a system to provide reliable quantitative data on distribution of activity in selected parts of the human body: each sensor in the system must record radiation only from a single, "it's own" region, i.e., there must be minimum contribution of radioactivity from an adjacent region; the effectiveness of recording per unit radioactivity distributed within the tested region must be the same for all sensors in the system.

Proceeding from these requirements, the optimum geometry for location of sensors and shields was established by means of theoretical and phantom experiments, and the required distance from the subject's body was determined.

The figure illustrates effectiveness of counting radioactivity as a function of the linear size of the tested region and distance to the body. As can be seen, mean margin of error in counting activity in selected regions does not exceed 5% when the detectors are 75 cm away. These estimates did not take into consideration the radiation from overlapping zones (double recording) that are hatched in the diagram. However, this additional radiation, which constitutes about 2% of the radioactivity of the entire region is compensated by a decrease in reading effectiveness due to the absorption effect, causing the recorded values to come closer to the true ones. The submitted estimates and arguments apply to relatively uniform distribution of activity in the tested region. In the event of extremely nonuniform distribution of activity, when two-thirds of it would be concentrated in the upper half and the remaining one-third in the lower half, with the reverse distribution of activity in adjacent regions, the margin of error in recording mean counting effectiveness will increase, but it will not exceed 8%. However, such a situation is virtually impossible.

The sensors and shields can move both vertically and horizontally, and they can take into full consideration individual anatomical distinctions of the subject. In addition, the entire installation can revolve about a central axis, to take care of any orthostatic or antiorthostatic position of the body; the system of sensors and shields moves together with the installation, so that a continuous record can be made of blood movement.

The system that has been developed permits performance of functional tests (LBNP, orthostatic test, physical loads, etc.) with continuous monitoring of blood movement. To assure reliability of radiometric readings, the system has an electronic device that is programmed for a set of optimum number of pulses (10,000 from the entire body), after which there is a digital print-out of information about the nature of distribution of existing volume of blood (plasma and erythrocytes) in regions (as percentages). Blood volume is determined when obtaining data in absolute units (milliliters) during testing of the process of blood distribution. Blood volume is determined repeatedly when studying the nature of blood movement during functional tests.

This device was tested for several years in various model experiments and has proven itself well.

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MUSCLE PRESERVATION IN THE STUDY OF BIOENERGETIC EFFECTS OF HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 15 Jan 87) pp 67-70

[Article by E. S. Mailyan and L. B. Buravkova]

[Text] When studying oxidative phosphorylation in skeletal muscles, a strict time limit on preparing tissue preparations is a mandatory prerequisite--respiration must be recorded no later than 1-1.5 h after decapitating the animal [2]. However, if animals are sacrificed outside the laboratory, or if a large number of tissue specimens need to be prepared at the same time, it becomes necessary to preserve tissue. Most studies in this direction are based on deep freezing (temperatures to -196°C) using solid carbon dioxide, liquid nitrogen, etc. It was shown that it is possible to preserve viability and functional activity of the chick embryo myocardium after immersion in liquid nitrogen with pretreatment with glycerin [6].

All these methods inevitably involve water-ice-water phase transitions. Use of even the most refined cryoprotective agents does not permit complete avoidance of the deleterious effect of crystallization of intracellular and extracellular fluid, which leads to dehydration of biomacromolecules and biological membranes, signs of osmotic shock, rupture and degradation of cytoplasm [5, 6]. Hence it becomes understandable that there are serious structural and functional disturbances of mitochondria, in particular, of the mechanism of energy transformation (depression of respiratory and phosphorylating activity, decreased cytochromoxidase activity) when freezing tissue sections in liquid nitrogen [6]. For this reason, a new direction has emerged--use of low-temperature tissue preservation in a nonfreezing aqueous medium. Thus, to preserve muscles of the large intestine a composition of medium and temperature began to be used that would not cause formation of crystals in either solution or the muscle [7, 8].

We shall deal here with development of a method of low-temperature preservation of skeletal muscles at subzero temperatures, which precludes the possibility of water crystallization. The method has to be suitable for preservation of pieces of muscles and subsequent study of processes of oxidative phosphorylation. We used 20% glycerin solution, which is the most effective cryoprotector with endocellular action [5], prepared on isolation medium (IM), so that there would be a balanced set of the most important electrolytes. Saccharose ice, prepared

from isotonic saccharose solution, which has been used with success for preservation of blood and myocardium [5], was used to store the material.

Methods

We conducted this study on 60 mongrel white male rats weighing 200-250 g. Muscles (posterior group of femoral muscles) removed following decapitation were loosened with a plastic dissecting needle and immersed in 20% glycerin solution prepared on IM cooled to -5°C. Pieces of muscles were kept in the glycerin solution for 30 min, then transferred into a thermos filled with chipped saccharose ice made from a saccharose solution of 0.25 mol/ℓ. If necessary, the biological material was transported and stored for 2-3 days in the thermos at temperatures of -7 to -1°C. At this temperature the 20% glycerin solution did not freeze, and muscles saturated with it and immersed in ice remained soft, did not change color, and there were no visible signs of crystallization in tissue fluid.

After 2 days, before isolating the mitochondria, glycerin was removed from the muscles by submersion in IM for 30 min. All of the procedures were performed at temperatures of -2 to +2°C. Differential centrifuging was used for isolation of mitochondria: 700 G for 7 min, 2000 G for 5 min, 12,000 G for 10 min. The IM was used to prepare muscle homogenates in a 1:5 ratio; its composition: 0.1 mol/ℓ KCl, 0.005 mol/ℓ $MgCl_2$, 0.05 mol/ℓ tris-HCl, 0.001 mol/ℓ EDTA, pH 7.5. The mitochondrial suspension was prepared in a medium containing 0.02 mol/ℓ tris-HCl, 0.3 mol/ℓ saccharose, 0.004 mol/ℓ EDTA and 0.1% albumin.

Conventional methods were used to determine the parameters of oxidative phosphorylation [2]. We measured rate of respiration in metabolic states 4p, 3 and 4o, as well as phosphorylation time (Δt). On the basis of these measurements, we calculated the respiratory control according to Lardi-Vellman (RC_l), respiratory control according to Chance-Williams (RC_c), ADP:O coefficient and phosphorylation rate (ADP:Δt). Mitochondrial protein content was measured according to Lowry [9]. Addition of mitochondria usually contained 2-3 mg protein per cell.

Results and Discussion

The table lists parameters of oxidative phosphorylation in mitochondria of muscles isolated immediately after decapitation and 2-3 days after the latter with use of muscle preservation. Analysis of the data revealed that prior long-term storage of muscles alters both intensity of respiration and parameters of coordination of oxidative phosphorylation. Thus, respiratory rate in different metabolic states diminished on the average by 35%, RC_l, RC_c, ADP:O coefficient and phosphorylation rate also decreased by 35%, while phosphorylation time increased by 1.5 times.

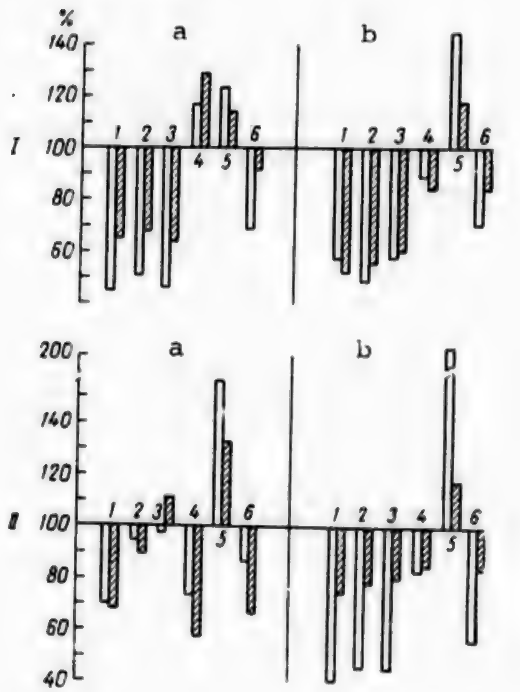
All this is indicative of some degree of diminished respiration and separation of oxidative phosphorylation in muscles after being stored.

We needed to determine the extent of these changes and whether such loss of initial native properties of muscles would distort the pattern of dynamic oxidative metabolism of muscles under extreme conditions, in particular, under the effect of long-term hypokinesia. For this purpose, we made a comparative study of oxidative phosphorylation during 20-day hypokinesia using two methods.

Characteristics of tissue respiration (nmol O_2/mg protein/min) of mitochondria of skeletal muscles isoalted by conventional method and following preservation of muscles ($\overline{X} \pm \sigma_x$)

Parameter	Oxidation substrate			
	succinate		α-ketoglutarate	
	CM	preservation	CM	preservation
V_4p	11,97±1,07 (36)	10,42±0,54 (55)	12,53±2,94 (14)	7,60±0,44* (33)
V_3	20,54±5,20 (27)	13,60±0,64* (48)	22,80±3,52 (13)	12,65±0,71* (33)
V_{4o}	15,21±1,54 (25)	11,04±0,65* (37)	19,05±3,30 (11)	10,34±0,61* (32)
RC_1	1,93±0,11 (29)	1,43±0,04* (48)	2,47±0,29 (13)	1,71±0,07* (33)
RC_c	1,55±0,11 (27)	1,23±0,03* (37)	1,35±0,09 (11)	1,25±0,03 (32)
ADP:O	0,76±0,07 (27)	0,47±0,03* (37)	0,64±0,08 (11)	0,53±0,04 (32)
Δ t, min	1,68±0,18 (26)	3,12±0,20* (37)	2,36±0,32 (11)	3,18±0,17* (32)
ADP:Δ t	73,36±6,84 (25)	39,65±3,54* (37)	53,49±8,80 (11)	35,56±2,32* (32)

Note: Number of animals is given in parentheses
CM) conventional method
*$p<0.01$



Deviation of oxidative phosphorylation parameters in experimental group of animals (hypokinesia) as related to control taken as 100%

I, II) 10th and 20th days

a) succinate b) α-ketoglutarate

In the first case, mitochondria were isolated from skeletal muscles immediately after decapitation; in the second, this was done 2-3 days later with use of the above-described method of preservation. Hypokinesia was produced by means of individual cages which restricted motor activity in all directions [1]. The following was established for the group of animals where the conventional method was used to isolate mitochondria. The 10th day of hypokinesia was associated with inhibition of respiration of mitochondria in different metabolic states with oxidation of different substrates: succinate and α-ketoglutarate, but parameters of oxidative

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← White bars--isolation of mitochondria without preservation; hatched--after preservation

1) V_4p
2) V_3
3) V_{4o}
4) ADP:O
5) phosphorylation time
6) phosphorylation rate

phosphorylation. At later stages (20th day), depression of respiration became less marked, but signs of free oxidation appeared: reliable increase in phosphorylation time and a tendency toward decline of ADP:O. The figure illustrates the extent of deviation of each parameter under hypokinetic conditions as compared to values obtained in the control group of animals using both methods of preparing tissue specimens. The data indicate that the changes in parameters of oxidative phosphorylation are in the same direction in the case of isolation of mitochondria without preservation and following preservation of muscles. In some cases, not only the direction, but quantitative expression of changes coincided. The patterns established for intact muscles were entirely reproduced with long-term low-temperature storage of skeletal muscles using the above-described method.

All this warrants the belief that use of this method of preserving muscles is justified for the study of energetic reactions in animal muscles in post-light studies aboard Cosmos-1129 and Cosmos-1514 biosatellites [3, 4]. This method of preserving muscles can, if necessary, be used in subsequent studies of animals flown aboard biosatellites, as well as in any other situations that require investigation of oxidative metabolism of skeletal muscles outside a laboratory and when processing a large number of blocks of muscle specimens within a short period of time.

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BRIEF REPORTS

UDC: 612.821.1/.3014.481:546.291

SHORT- AND LONG-TERM EFFECTS OF NONLETHAL LEVELS OF FAST HIGH-ENERGY HELIUM IONS ON RETENTION OF DEVELOPED AND FORMATION OF NEW BEHAVIORAL PATTERNS IN RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 4 Mar 86) pp 70-72

[Article by N. Ya. Savchenko]

[Text] Most published studies [1, 3, 5-7] were pursued with use of various doses of x-, gamma and gamma-neutron radiation. However, there are only a few morphological studies of the effect on the central nervous system of heavy charged particles with different energy and linear energy transfer (LET) [9].

Our objective here was to investigate the effect of fast helium ions with energy of 4 GeV/nucleon. We used rats in our study, and retention of developed behavioral skills and formation of new ones at the short and long terms following nonlethal exposure in a changing situation with increased sensory input served as our criteria in assessing the effects. It has been shown in studies of the effects of radiation and nonradiation factors on higher nervous activity [7, 8] that investigation of rat behavior in a complicated maze is an integral parameter that yields rather complete information about the function of the CNS [central nervous system].

Methods

Experiments were conducted with adult male Wistar rats. In order to develop a conditioned motor chain reflex we used the Dombrovskaya maze [4]. To complicate the situation, which causes more complete demonstration of work capacity of higher branches of the CNS and assess the top range of its capabilities, we used the following methods: stress factor (20-s exposure to 3000-Hz sound after starting the test), increasing the number of presentations of the task, changes in a specific order of the system of paths, locked and unlocked doors, open gates and dead ends ("skill changing" test). The rats were conditioned in the experimental device daily; stable 100% performance of the test consisting of three presentations was considered the criterion of a reinforced skill. We recorded the latency period of responses, number of instances of complete absence of reflex (refusals), locomotor response time, total reflex time and mean number of mistakes. Motor activity was evaluated according to distnace traveled in the maze [8]. The rats were exposed to total-body fast helium ions with energy of 4 GeV/nucleon

in a dosage of 5.0 Gy. Dose rate was 0.003 Gu/s, beam homogeneity 10% at LET of 0.88 keV/ m. A control group of animals was exposed to pseudo-radiation under close to experimental conditions. Each group consisted of eight rats that had been selected and trained before the experiment. The integral behavioral effect was examined 6, 24 h, 5-7, 10, 20, 30 days, 1.5, 3 and 6 months after exposure. The obtained data were processed using the U criterion of Wilcoxson-Mann-Whitney [2].

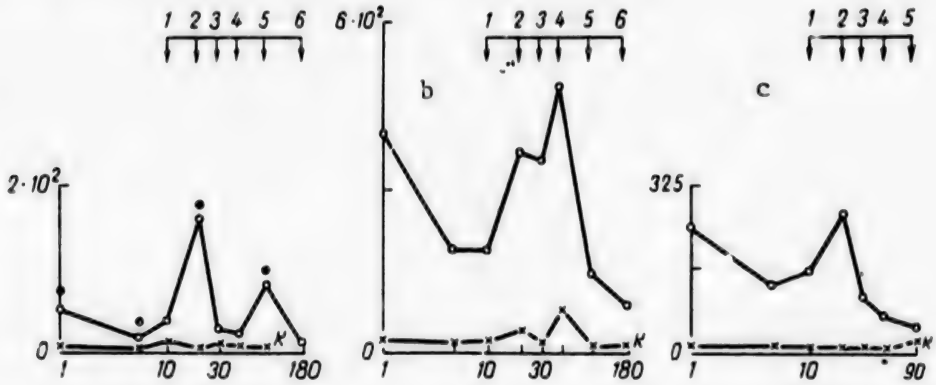

Figure 1. Retention of existing and development of new behavior in rats following exposure to 5.0 Gy fast helium ions

X-axis, tested time (days); y-axes:

a) mean latency period (s) c) mistakes made (%)

b) locomotor response time (s)

•--probability of reliability of differences ($p<0.05$)

Arrows at the top show: 1) audio stimulus

2) 16 runs in maze

3-6) alteration of skill

Here and in Figure 2, κ refers to the control group.

Results and Discussion

Worsening of reflex activity was demonstrated 6 and 24 h after irradiation; it was manifested by an increase in number of mistakes, prolongation of mean latency period, increased locomotor response time (see Table and Figure 1). A decrease in number of mistakes, latency period and locomotor response time was observed 5-7 days after irradiation (see Figure 1). The animals were active, groomed, ate willingly and did not refuse to perform the task. The audio stimulus used on the 10th day led to marked impairment of behavioral responses with development of rather profound inhibition at the time of delivery of the signal followed by development of generalized motor excitation after discontinuing the audio stimulus. Worsening of reflex activity was manifested by an increase in number of mistakes with decline in level of preservation of acquired skill: the ratio of mean number of mistakes in the third presentation of the task to the number of mistakes after the first run showed a reliable 2.7-fold increase, as compared to the control. Use of the test, which involved 16 presentations of the task instead of the usual 3, led on the 20th postradiation day to increase in latency period, locomotor response time, total reflex time, as well as change in motor activity, increase in percentage

of mistakes and dramatic decline of level of retention of acquired skill (see Figures 1 and 2). Use of the "skill alteration" test after 1, 1.5, 3 and 6 months revealed development of compensation of impaired connecting function of the cortex at the late and long terms following irradiation.

Characteristics of behavioral responses of rats in Dombrovskaya maze 6 h after exposure to high-energy fast helium ions in a dose of 5.0 Gy

Parameter	Irradiated animals	Control
Motor activity, number of maze compartments	59.5	58.6
Mean number of mistakes	11.4**	5.4
Impairment of skill, %*	162.5**	30.2
Latency period, s	10.8	11.5
Total reflex time, s	304.5	129.7
Alimentary activity, %	83.3	97.8

*Ratio of mean number of mistakes made by animals in third run in maze to number of mistakes in first run.

**$p<0.05$

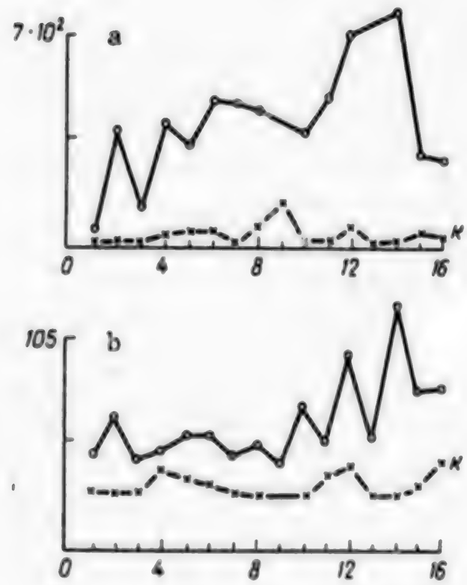

Figure 2.
Motor activity of rats on 20th postradiation day, exposure to high-energy helium ions in dose of 5.0 Gy, with presentation of increased functional load; x-axis, number of task presentations; y-axis:

a) mean locomotor response time (s)
b) distance traveled in maze, number of compartments

Thus, at the early stages following exposure to fast high-energy helium ions in a dosage of 5.0 Gy, we demonstrated a phasic pattern of changes with depression of reflex activity within 24 h. Restoration of some CNS functions, which occurred in the first week, was indicative of development of compensatory processes. However, the increased latency period, total response time and high percentage of mistakes were indicative of functional weakness of cortical processes. Depression with dramatic increase in excitability in response to an audio stimulus was indicative of pathological lability with prevalence of an excitatory process [7]. Use of functional loads revealed some decline of work capacity. However, at the late postradiation stage we observed development of recovery processes with compensation of impaired functions.

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MYOSIN Ca^{2+}, Mg^{2+}-ADENOSINE TRIPHOSPHATASE ACTIVITY IN RAT MYOCARDIUM FOLLOWING THIRTY-DAY EXPOSURE TO 1.1 AND 2.0 G

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, Sep-Oct 87 (manuscript received 4 Jan 87) pp 72-74

[Article by I. B. Krasnov and Ye. A. Nosova]

[Text] The decline in myosin Ca^{2+}, Mg^{2+}-ATPase in the myocardium of rats flown in space for 18.5-22 days aboard Cosmos series biosatellites [1-3, 9] is viewed as the consequence of absence of sufficient load on the muscular system of the heart in weightlessness, and it is assessed as one of the manifestations of mammalian adaptation to this state. Data concerning the level of activity of myosin Ca^{2+}, Mg^{2+}-ATPase in the myocardium of rats exposed to both hypergravity (HG) produced during rotation on a centrifuge and relatively reduced gravity (RRG) [6] would be of considerable interest with respect to broadening our ideas about the possibility of adaptation of mammals to altered gravity. RRG is viewed [6] as a state that arises as a result of reduction in weight (but not mass) of an organism following change from hypergravity, to which the body adapted, to earth's gravity. The RRG state apparently lasts until there is adaptation to earth's gravity of receptor structures that perceive changes in gravity, as well as structures of the nervous and endocrine systems that form the body's response to change in gravity. It can be assumed that the changes arising in weightlessness and RRG in structures and systems that perceive change in gravity and effect adaptation to this change will be in the same direction.

Our objective here was to examine the activity of myosin Ca^{2+}, Mg^{2+}-ATPase in the myocardium of rats submitted for 30 days to HG of 1.1 and 2.0 G, as well as RRG for 2 days after discontinuing exposure to the above level of gravity for 30 days.

Methods

The rat myocardium was isolated in an experiment that has been described in detail previously [6]. HG was produced for 30 days by rotation on a centrifuge in its peripheral (P group) and central (C group) segments at 2.0 and 1.1 G, respectively. On the 30th day of rotation and 2d day after it was stopped (2d day of RRG) groups P, C and vivarium control (K) rats were decapitated. After decapitation, the myocardium was extracted, blood drained from it, and a fragment was excised from the left ventricular wall; it was

frozen in liquid nitrogen and stored at -40°C. For isolation of myofibrillar proteins, the fragment of the left ventricular wall (300-400 mg) was macerated in liquid nitrogen and then treated according to Solar in the modification of Saks et al. [8]. Myosin Ca^{2+}, Mg^{2+}-ATPase activity was determined according to build-up of inorganic phosphate [16] following 10-min incubation at 30°C in a medium containing 20 mM imidazole, 50 mM KCl, 2 mM $MgCl_2$, 2 mM ATP, 0.1 mM $CaCl_2$ and 5 mM dithiothreitol at pH 7.0. Protein was assayed according to Lowry [14].

Results and Discussion

There was 2-fold increase in activity of myosin Ca^{2+}, Mg^{2+}-ATPase in the myocardium of rats submitted to 2.0 G for 30 days, as compared to activity of this enzyme in the K group of animals (see Table). Previously, an increase in activity of this enzyme in the rat myocardium was demonstrated after exercise--swimming [12, 13] and running on a treadmill [5], as well as after daily 25-min exposure to 5 G for 14 days [9]. Myosin Ca^{2+}, Mg^{2+}-ATPase activity in the myocardium determines the rate and amplitude of contractions of the myocardium [7, 11], and an increase in activity of this enzyme apparently indicates that there is an increase in rate and amplitude of cardiac contractions in rats exposed to 2.0 G. Since increase in stroke volume (SV) and cardiac output (CO) is based on increase in rate and amplitude of myocardial contraction, it can be assumed that SV and CO are increased in the P group of animals. This assumption is all the more warranted since there has to be dramatic increase in resistance to ejection of blood from the left ventricle into the aorta when rats are exposed to 2.0 G and, consequently, when there is 2-fold increase in weight of blood. As shown in experiments with the rat heart [7], elevation of pressure in the aorta (increase in resistance to ejection of blood) elicits increase in SV and CO.

Activity of myosin Ca^{2+}, Mg^{2+}-ATPase (in nmol P_n/mg protein/min at 30°C; M±m) in myocardium of rats submitted to HG

Group of animals	Stage of experiment	
	30th day of HG	2d day of RRG
K	76±10 (5)	68±8 (5)
C	55±5 (4)	62±6 (4)
P	153±37*(7)	76±5 (5)

*p<0.01, as compared to control.
Note: Number of animals is given in parentheses.

On the 2d day of RRG, the P group of rats showed a decline in activity of myosin Ca^{2+}, Mg^{2+}-ATPase to the level inherent in the K group, which is indicative of decline in rate and amplitude of cardiac contractions and implies a decrease in SV and CO in response to the diminished weight of blood after HG. It should also be noted that the changes in activity of this enzyme in the rat myocardium on the 2d day of RRG and following 18.5-22 days in weightlessness are in the same direction. However, on the 2d day of RRG, activity of myosin Ca^{2+}, Mg^{2+}-ATPase diminishes, as compared to activity on the 30th day of HG only to the level of activity of this enzyme in the K group, i.e., to the level inherent

in conditions of earth's gravity, whereas in weightlessness activity of this enzyme in the rat myocardium was 33-55% lower than its level in the K group [1-3, 9]. The decline in activity of myosin Ca^{2+}, Mg^{2+}-ATPase in the myocardium to values below the level inherent in earth's gravity is due to the effect of expressly weightlessness, since artificial gravity produced by rotation on the onboard centrifuge on Cosmos-936 inhibited this process [9], while 30-day hypokinesia in the ground-based experiment did not alter activity of this enzyme [5]. The fact that activity of this enzyme in the rat myocardium diminishes in weightlessness enables us to expound the hypothesis that SV and CO decrease in response to weightlessness of circulating blood during flight aboard the biosatellite.

In group C rats submitted for 30 days to 1.1 G, activity of myosin Ca^{2+}, Mg^{2+}-ATPase showed virtually no change. Apparently, an 0.1 G increase in gravity, as compared to earth's gravity, is insufficient to produce a load on the myocardium that would require increase in activity of this enzyme. It must be noted that exposure of rats to 1.4 G during 18.5-day rotation on a centrifuge in the ground-based synchronous experiment conducted as a control for the experiment with rats aboard Cosmos-936 [4] was also insufficient to increase activity of myosin Ca^{2+}, Mg^{2+}-ATPase in the myocardium [9].

Myosin Ca^{2+}, Mg^{2+}-ATPase effects hydrolysis of ATP, providing for utilization of the energy of the macroergic phosphate bond of ATP for a mechanical process--contraction of actomyosin fibrils. The level of its activity is determined by the ratio, in the myosin S fragment, of long-lived, light L to short-lived, heavy H polypeptide chains, the relative prevalence of the former being associated with decrease in enzyme activity, while prevalence of the latter is associated with increase [15, 17]. More probably, the ratio of L to H chains is determined by the ratio between rates of synthesis and dissociation of short-lived H chains, rather than long-lived L chains, and for this reason it can be assumed that the molecular mechanism, upon which is based the increase in activity of myosin Ca^{2+}, Mg^{2+}-ATPase in the rat myocardium in HG, consists of prevalence of synthesis of H chains. The decline in activity of this enzyme on the 2d day of RRC, as well as in weightlessness, can apparently reflect the decline in rate of synthesis of polypeptide H chains.

Thus, the demonstrated increase in myosin Ca^{2+}, Mg^{2+}-ATPase activity in the myocardium of rats submitted to HG, as compared to data concerning decline in activity of this enzyme in the myocardium of weightless rats, warrants the belief that the change in activity of this enzyme is one of the molecular mechanisms of myocardial adaptation to two opposite states--hypergravity and weightlessness--with opposite direction of action of this mechanism in the two states.

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KINETIC TOXIC ASPECT OF POTENTIAL USE OF SULFUR HEXAFLUORIDE IN CLOSED ENVIRONMENTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 28 Jul 86) pp 74-77

[Article by S. S. Pashin, V. F. Ushakov, A. I. Gorshunova, N. Ye. Ostasheva, Ye. B. Stadukhin and E. I. Chukhno]

[Text] Heretofore, the effect on the body of sulfar hexafluoride (SF_6 gas, SF_6) was attributed to its use as an experimental model in the study of the effects of high density gas enivornment on respiration under hyperbaric conditions [15, 1]. The prospects of using SF_6 gas in the atmosphere of closed environments as a means of extinguishing fires, which involve the possibility of the dirrect effect of SF_6 on man under extreme conditions, made it necessary to submit this compound to comprehensive hygienic evaluation.

Sulfur hexafluoride is a compound with low toxicity. The absence of deaths of experimental animals, even with use of maximum possible concentrations (80 vol.%) and long exposure time (up to 24 h), led to the conclusion that pure SF_6 gas is nontoxic, and that the presence of toxic admixtures could be the adverse factor with respect to health [13, 11]. However, there is information in the literature that does not allow us to consider pure SF_6 gas to be a neutral substance. A response was noted with reference to parameters of rabbit peripheral blood after 1-h exposure to sulfur hexafluoride in concentrations of 1.25-1.7 vol.%. In the cited authors' opinion, the decline in red blood cells and hemoglobin was related to the destructive effect of SF_6 gas on hemoglobin and erythrocytes [6].

Histological changes in mouse viscera (brain tissue, liver, kidneys) were found in experiments involving 8- and 24-h exposure to SF_6 in a concentration of 80 vol.% [4].

Single exposure to SF_6 gas in concentrations of 1500 and 300 g/m^3 (23 and 4.6 vol.%) led to decline of functional parameters of the central nervous system (CNS) of experimental animals. With chronic exposure to this compound in concentrations of 77 and 9,8 g/m^3 (1.2 and 0.15 vol.%), in addition to its effect on the CNS, there was a decline in renal function and an insignificant response of parameters of peripheral blood [5]. A concentration of 5 g/m^3 (0.08 vol.%) was approved as the maximum permissible concentration of SF_6 in work zone air.

We shall be dealing here with questions related to intake, distribution and elimination of SF_6 gas which have not been covered in the literature.

Methods

The studies were conducted on 45 mongrel, male white rats and 25 male Wistar rats. During the inhalation period, the animals were in a steel 14-ℓ chamber. A dynamic method was used to generate the concentrations of SF_6 by means of continuous pumping through the chamber of air from elastic containers with a mixture of the required amounts of SF_6 gas and oxygen prepared in advance.

To examine the nature of distribution and elimination of SF_6 the animals were sacrificed by decapitation. Use of this method in experiments dealing with the study of kinetics of intake of the substance was difficult, not only because it was necessary to conduct studies after prolonged, but also after short-term exposure, when the time required to remove animals from the chamber and decapitate them was comparable to duration of exposure. To improve the accuracy of obtained results at this stage of the experiment, the animals were sacrificed in the chamber by means of producing an anoxic gas atmosphere in it. The design and size of the chamber, combined with the feasibility of increasing significantly air exchange, provided for very rapid replacement of the gas atmosphere in the chamber and onset of death of all experimental animals within 10 s from the time that we began to alter the gas composition, which enabled us to use 100% SF_6 gas as the anoxic environment. A brief change in SF_6 concentration in inhaled air did not affect its overall level in the body (tissue) after exposure, due to the low solubility of this compound in blood. Samples of exhaled air were collected by means of a cone-shaped metal mask equipped with "inspiration" and "expiration" valves [9].

Concentrations of SF_6 gas in exhaled and inhaled air were determined using a Tsvet-100 chromatograph. A katharometer was used as a detector. A chromatographic column 2 m in length was filled with KCM siliga gel (0.5 m) and CaA (1.5 m) molecular sieves. Column temperature was 20°C, temperature for delivery of sample was 60°C and for the detector 40°C. The rate of helium flow was 40 mℓ/min, and sensitivity of the method was $0.12 \cdot 10^{-3}$ vol% (1-m samples). SF_6 gas content in the biological specimens was measured on a Shimadzu GC-1c chromatograph with tubular pyrolytic attachment. The method is based on direct thermal evaporation of chemicals from the specimens placed in a sealed quartz tube (volume 5 m) of the pyrolytic attachment followed by analysis of the gas phase [8]. A katharometer was used as a detector. The chromatographic column was filled with 13x molecular sieves (0.25-0.5 mm fraction). Column temperature 90°C, specimen input and detector temperature 120°C. The rate of helium flow was 30 mℓ/min. Sensitivity of the method 0.09×10^{-3} mg% (150-300 mg batch of biological specimens).

Results and Discussion

Investigation of the distribution of SF_6 gas in experimental animals revealed that the amount of this compound in tissues corresponded to the level of its solubility in water and lipids. In spite of its low solubility in blood, sulfur hexafluoride accumulated in significant amounts in fatty tissue. Somewhat more SF_6 gas was deposited in fatty tissue near the kidneys (per unit

mass) than in the subcutaneous fatty tissue. Maximum concentration of SF_6 following 5-h exposure to a concentration of 80 vol% reached $183 \cdot 10^{-3} \pm 12.5 \cdot 10^{-3}$ mg% in the perirenal fatty tissue. SF_6 content in tissues of the spinal cord, brain and blood constituted 14, 4 and 0.5%, respectively, of its level in fatty tissue. SF_6 was demonstrable in tissues of other organs (liver, kidneys, spleen, heart, lungs and others) only at the level in blood or below this level. For this reason, one can judge the amount of SF_6 gas in the body as a whole on the basis of its accumulation in fatty tissue. We should call attention to the fact that SF_6 concentration in the spinal cord was 3.5 times higher than in the brain. Interestingly enough, an analogous finding was made with respect to levels of dichloroethane in the spinal cord and brain [7]; this is a substance that is also soluble in lipids. According to the results of these studies, the concentration of dichloroethane in the spinal cord and brain constituted 0.7 and 0.14-0.2%, respectively, of its content in blood. Comparative analysis of experimental data referable to different substances indicates that the distribution of fat-soluble substances in tissues of different parts of the CNS is stable. Differences in distribution of SF in experimental animals could be due to differences in amounts of fats and lipids in tissues, as well as differences in their physicochemical properties.

The mechanism of biological action of SF_6 gas can be attributed to its physical properties. Having a high density, this compound enhances resistance to respiration, as a result of which hypoxemic and hypercapnic changes may be seen [12, 14], the severity of which would depend on the level of motor activity [1]. Hence, the response referable to parameters of peripheral blood and the CNS is understandable. We were impressed by the possible link between CNS sensitivity to sulfur hexafluoride (even in rather low concentrations) [5] and relatively high level of this compound in tissues of the spinal cord and brain, which does not rule out the existence of a direct effect of SF_6 on functional state of the CNS.

Solubility in fats, which is one of the basic conditions for penetration of substances through the integument prompted investigation of the routes of intake of sulfur hexafluoride [2]. As shown by experiments, in which animals breathed pure air, while most of their body was in an atmosphere of 100% SF_6 gas, the latter was not demonstrable in either perirenal fatty tissue or subcutaneous fatty tissue, even after 5-h exposure, which precluded the possibility of penetration of this compound into the body, except the lungs.

The kinetics of intake of chemicals is usually described by an exponential equation of the following general appearance:

$$C = \lambda C_0(1-e^{-kt}) \text{ [10]},$$

where C is substance concentration in a biological specimen in time t, C_0 is substance concentration in the ambient environment, λ is the coefficient of distribution of substance in the biophase and surrounding medium, k is accretion constant, e is the base of a natural logarithm. In our studies, an exponential intake of SF_6 gas was observed only at the second stage of exposure. At the first stage, during 1-h inhalation, the kinetic of accumulation of substance as a function of time corresponded to a quadratic function. In its general form, the nature of accumulation of SF_6 gas in animals during

inhalation can be graphically depicted by an S-shaped curve (Figure 1). The results of the studies made it possible to offer a mathematical description of accumulation of sulfur hexafluoride at the first stage of exposure in the form of the following equation:

$$C = (20\ C_0{}^2 t)^2 + 20\ C_0{}^2 t$$

where C_0 is SF_6 concentration in inhaled air ($\cdot 10^{-3}$ vol.%), C is concentration of SF_6 gas in the biological sample ($\cdot 10^{-3}$ mg%) after t min. Using this equation, one can calculate the levels of exposure to sulfur hexafluoride at which its accumulation in the body will be insignificant. For example, with 2-h and 3-week exposure to SF_6 in concentrations of 5 and 0.2 vol%, respectively, the amount of this substance in animals should, according to the equation, be beyond the range of sensitivity of the analysis method used. Experiments performed at the above levels of exposure confirmed this assumption--no SF_6 gas was detected in the animals.

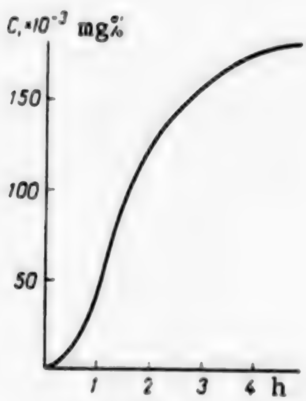

Figure 1.

Kinetics of accumulation of SF_6 gas in rats during inhalation
X-axis, inhalation time (h); y-axis, concentration of SF_6 gas in rat fatty tissue ($\cdot 10^{-3}$ mg%)

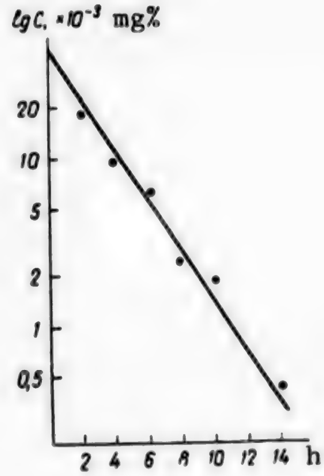

Figure 2.

Kinetics of elimination of SF_6 gas from rats after exposure
X-axis, time after inhalstion (h); y-axis, common logarithm of SF_6 concentration in rat fatty tissue ($\cdot 10^{-3}$ mg%)

The existence of accumulation of substance as a quadratic function of inhalation time is apparently related to the fact that deposition of SF_6 gas does not occur in fatty tissue in general, but specifically in fat cells (adipocytes) surrounded by cells of friable connective tissue. Fatty tissue can be arbitrarily divided into two parts according to solubility of this compound: fatty site of deposition and connective tissue. The fatty deposition site is surrounded by connective tissue and has no direct contact with blood, which is the carrier of sulfur hexafluoride in the body. For this reason, the rate of accumulation of the substance in the fatty reservoir will depend on extent of saturation with this compound of surrounding connective tissue. With exponential saturation of connective tissue with SF_6 gas, the rate of its penetration into the fatty reservoir will increase constantly and its concentration

will grow in accordance with an exponential function of time. This process is extended in time due to the low solubility of this compound in water. After connective tissue is saturated with sulfur hexafluoride, the rate of its penetration into the fatty reservoir levels off, and its further accumulation there (and consequently in fatty tissue as a whole) is exponential, as is inherent in accumulation of chemicals in a biological substrate.

The considerable accumulation of sulfur hexafluoride in experimental animals made it necessary to conduct a comprehensive study of the kinetics of elimination of this compound in order to assess the biological significance of tangible accumulation. Tangible accumulation may be dangerous if the rate of intake of the substance exceeds significantly the rate of its elimination. Moreover, the kinetics of elimination of a substance from the body may be governed by a two- and even three-exponent function, rather than one exponent. Thus, according to data in the literature, after exposure to arsenic trioxide, 60% of the arsenic was eliminated with a half-life of 2.4 days, 29% with a half-life of 5.4 days and 11%, 17.2 days [3]. Hence the danger that tangible accumulation could present is understandable, particularly in the case of repeated exposure.

Investigation of kinetics of elimination of SF_6 from experimental animals after 1-h exposure to this compound in a concentration of 70 vol.% revealed that the concentration of SF_6 constituted ($\cdot 10^{-3}$ mg%) 44.3±8.3 immediately after exposure, 18.9±1.1 2 h after exposure, 9.4±0.91 after 4 h, 5.93±2.5 after 6 h, 2.37±1.4 after 8 h, 1.77±0.8 after 10 h, 0.41±0.1 after 14 h, and none was demonstrable after 24 h. These figures characterize the levels of SF concentrations only in the perirenal fatty tissue since, as we have already indicated, this tissue is the principal reservoir for the substance in question, and already 2 h after exposure this compound was not demonstrable anywhere except fatty tissue.

Analysis of the experimental data revealed that the kinetics of elimination of sulfur hexafluoride can be described by the following equation:

$$C = C_0 e^{-0.362\,t}$$

where C_0 is the initial concentration ($\cdot 10^{-3}$ mg%), C is concentration ($\cdot 10^{-3}$ mg%) t h after exposure. Graphically this function is a straight line in a semilogarithmic system of coordinates (Figure 2).

The decline in SF_6 concentration in exhaled air was also exponentially a function of aftereffect time, in accordance with the following equation:

$$C = C_0 e^{-0.362\,t}$$

where C_0 is initial concentration ($\cdot 10^{-3}$ vol.%), C is concentration ($\cdot 10^{-3}$ vol.%) t min after exposure. Maximum concentration of SF_6 gas in exhaled air did not exceed 0.05 vol.%.

These studies enable us to draw the conclusion that, considering the presence of a one-exponent function for kinetics of elimination and relatively short half-life, tangible accumulation of SF_6 does not present an increased danger. Its concentration when actually used in the atmosphere of closed environments

would constitute relatively low levels that would not cause perceptible accumulation of this compound in the body. In addition, it should be borne in mind that the parameters of toxicokinetics of sulfur hexafluoride were determined in experiments with rats, whose metabolism is considerably higher than in man, and for this reason, the rate of accumulation of this compound in man would be slower.

At the same time, in spite of the low toxicity, repeated exposure to sulfur hexafluoride is undesirable (particularly in relatively high concentrations) at intervals of less than 24 h, since otherwise there could be incomplete elimination of residual amounts of the substance and, consequently, tangible accumulation could change to functional accumulation, since we cannot rule out the direct biological effect of this compound.

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COMPARATIVE EVALUATION OF ORTHOSTATIC STABILITY FOLLOWING IMMERSION IN HORIZONTAL AND VERTICAL POSITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 10 Feb 87) pp 77-79

[Article by A. Yu. Modin]

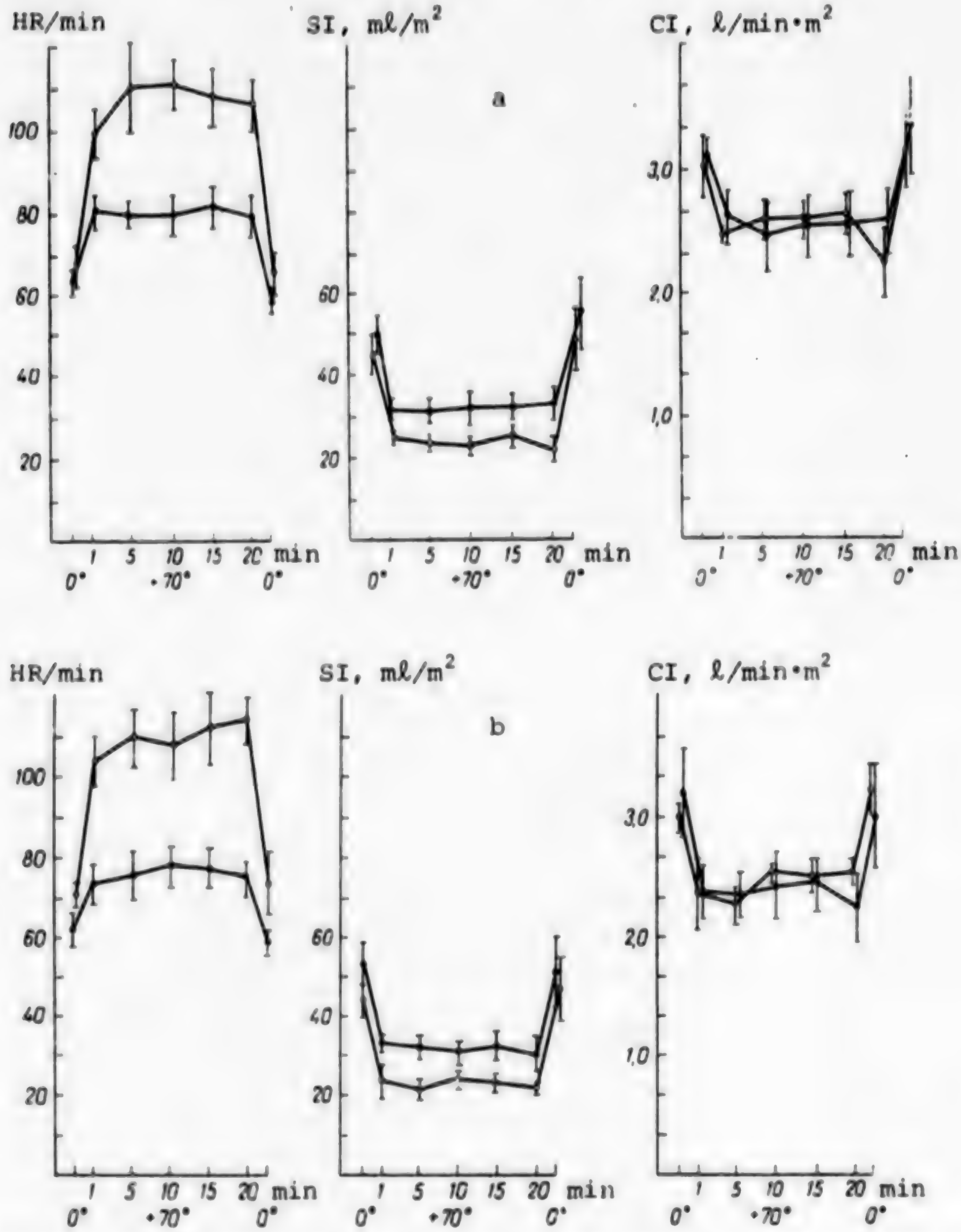
[Text] Among methods for ground-based simulation of weightlessness, the anti-orthostatic variant of bedrest [head-down tilt] and water immersion have gained the greatest popularity. The redistribution of fluids and hypodynamia syndrome that are thus simulated are based on various mechanisms. While simulation of these effects by the "antiorthostatic" method imposes certain requirements as to position and locomotor activity, these requirements are not as apparent. Theoretically, it could be assumed that compensation of gravity by the ejecting force of the immersion medium levels off both posture-dependent hemodynamic effects of gravity and antigravity component of work associated with motor activity. In particular, there is information to the effect that there is virtually the same polyuric response in horizontal and vertical positions during immersion [3]. This warrants the assumption that the nature of distribution of circulating blood does not change appreciably when body position is changed in the immersion medium. If this hypothesis is valid, a change in orientation of the immersed body should also not affect the extent of subsequent deconditioning of the cardiovascular system with respect to an orthostatic factor. However, we did not encounter any indications in the literature concerning direct evaluation of orthostatic stability in the aftereffect period following vertical immersion. Our objective here was to make a comparative study of the effect of immersion in horizontal and vertical positions on orthostatic resistance of man.

Methods

These studies were pursued on 6 essentially healthy male volunteers 23-34 years of age. Each subject was submitted to water immersion twice for 3 days, retaining horizontal orientation of the body throughout the exposure time (first series of tests) and vertical orientation (second series). There was an interval of at least 60 days between series.

One day before immersion and immediately after it, in both series of studies we performed a 20-min orthostatic test by means of passive change to close to vertical position (+70°). We used the rheographic method of Kubichek as modified by A. M. Genin et al. [1] to examine central hemodynamics. We determined

heart rate (HR), stroke (SI) and cardiac (CI) indexes. Statistical processing involved computation of means and their errors, as well as estimation of reliability of differences using Wilcoxson's paired T criterion.



Parameters of central circulation before and after 3-day immersion in horizontal (a) and vertical (b) positions

X-axis, min in orthostatic position.

●--before immersion, ○--after immersion

Results and Discussion

According to the results of baseline (before immersion) ortho-clinostatic testing, all of the subjects in both series had good initial orthostatic stability. With passive change to orthostatic position, HR increased by

25.3% in the first series of tests and 25.4% in the second, while SI decreased by 36 and 40.5%, respectively. The CI decline constituted 19.7% in the 1st series and 25.4% in the 2d. Absolute values of recorded parameters showed virtually no differences in both series in the baseline period (see Figure).

After immersion, regardless of immersion variant, deadaptation of the circulatory system to function in erect position was manifested mainly by typical change in correlation between CI components: increase in HR and decrease in SI, the characteristics of overall volumetric blood flow showing virtually no change. The orthostatic HR increment after the recumbent variant of immersion constituted a mean of 59.5% and increased in each subject, as compared to the baseline ($p<0.01$). Following vertical exposure, orthostatic HR increment increased in 5 out of 6 cases ($p<0.05$) and constituted a mean of 57.2%. The decrease in SI related to passive change to orthostatic position was more marked after immersion. While the postural decline of SI exceeded 40% in only 3 out of 12 cases in the baseline period in both series, after immersion the decline of SI constituted a mean of 50.9% in the 1st series and 48% in the 2d, and in only 1 of all the cases was the orthostatic decline of SI below 40%. Absolute values for HR and SI before and during the entire postimmersion test were virtually the same in both series (see Figure).

Clinical observations and subjective reports of the subjects were indicative of marked symptoms of diminished orthostatic stability. In 2 cases, the latter was extremely marked, as manifested by signs of impending collapse in the 10th-12th min of the test (in 1 case after the recumbent variant and in the other after the vertical variant of immersion). In the rest of the subjects, regardless of type of immersion, signs of deconditioning ranged from subjective perception of the test as a greater functional load to unpleasant sensations of vegetative discomfort that occurred episodically during the study.

Thus, are findings are indicative of absence of appreciable differences in extent of deconditioning effect of both variants of immersion. Quantitative dynamics of recorded parameters virtually corresponded to the changes noted in "dry" immersion of the same duration [2] with subjects in recumbent position. According to the submitted data, adherence to a strictly fixed longitudinal position of the body during immersion in relation to the vector of gravity is not a mandatory condition for reproducing orthostatic intolerance as one of the requirements for adequate simulation of weightlessness.

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COMPARATIVE EVALUATION OF STRESS RESPONSE OF RATS TO DIFFERENT METHODS OF SIMULATING SOME EFFECTS OF WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 5 Sep 86) pp 79-81

[Article by G. N. Durnova, Ye. V. Vorotnikova and N. G. Prodan]

[Text] When simulating some of the effects of weightlessness by means of restricting movements or "suspension," rats present an acute stress response, the severity and duration of which vary appreciably, depending on the chosen model of weightlessness. We have made a comparative evaluation of the stress reaction, using morphological methods, to the most widely used methods of simulating weightlessness, and we judged the nature and severity of this response according to changes in the adrenals and lymphoid organs that depend on them.

Methods

An experiment was performed on 38 male Wistar rats initially weighing 180±5 g. Ten of them were sacrificed before the start of the experiment (1st group), 10 rats were placed in tight box-cages for 7 days (2d group), 8 animals were suspended for 7 days by the tail in head-down position by the method of Ye. A. Ilyin and V. Ye. Novikov [1] (3d group) and 10 rats were kept in the vivarium throughout the experiment (4th, control group). Upon termination of the experiment, the animals were weighed, decapitated in a guillotine, their adrenals, thymus and spleen were extracted and these organs were weighed. For a comparative study of lipid content, 3 adrenals (one from each experimental group and the control) were mounted per block holder from the microtome-cryostat, quickly frozen in dry ice, after which sections were prepared in the cryostat and fixed in 10% neutral formalin. Adrenal lipids were demonstrated using oil red O and sudan black B. Adrenals to be submitted to histological examination were fixed in Wood's fixative, imbedded in paraffin and sections were stained with hematoxylin and eosin. Thymus and spleen specimens fixed in Carnoy fluid and 10% neutral formalin were imbedded in paraffin; sections were stained with hematoxylin and eosin, methyl green-pyronine and by the Perls method for iron. The digital data were submitted to statistical processing according to Student.

Results and Discussion

The table lists the results of measuring the weight of the animals, adrenals and lymphoid organs. According to the listed data, the 3d and 4th groups of rats continued to grow during the experiment. Their weight gain in 7 days was 11 and 16% greater than in the 1st group. At the same time, the 2d group of rats stopped gaining weight. A comparison of weight of experimental groups of animals to the vivarium control revealed that the weight of animals in the 3d group was was virtually the same as for those in the 4th group, whereas the 2d group weighed reliably less than the latter. The weight of the adrenals, thymus and spleen of the 3d group of rats did not differ from the parameters for the 4th group, although they did show a tendency toward a greater adrenal weight and lower thymus weight. The 2d group of animals showed a decrease in thymus and spleen weight: absolute weight of adrenals in this group did not change, whereas relative weight increased.

Effect of 7-day hypokinesia and "suspension" on weight of body, adrenals and lymphoid organs of rats

Group	Wt., g	Adrenals		Thymus		Spleen	
		mg	mg/100 g	mg	mg/100 g	mg	mg/100 g
1	179±5	31,7±2,4	16,0±0,9	325±25	175±17	555±25	300±17
2	179±5**	36,1±3,8	19,0±1,4**	189±23*,**	99±13*	525±23**	288±13
3	198±4*	39,7±3,8	18,0±1,2	241±48	112±17*	596±42	292±19
4	208±8*	32,8±1,8	16,0±0,7	301±41	147±20	641±49	315±31

*Reliable differences as compared to 1st group.
**Reliable differences as compared to 4th group.

Histochemical study of lipid content of the adrenals of rats in the 4th group revealed that lipid drops were demonstrable in cells of the upper third of the reticular, fascicular and glomerular zones of the cortex. In the reticular and lower third of the fascicular zones there was prevalence of small and medium-sized drops, whereas in the upper parts of the fascicular and in the glomerular zones there were large drops of lipids. A sudanophobic layer was demonstrable in all animals. In the 3d group, lipids were demonstrable in all zones of the adrenal cortex, including the entire reticular zone where there were many fine droplets of lipids; there was no sudanophobic layer in the adrenals. No signs of hypertrophy of the fascicular zone or structural alteration of cortical substances of the adrenals were observed in the 3d group of rats. Unlike the parameters for this group of animals, most of those in the 2d group showed no lipids at all in either the reticular or lower third of the fascicular zone. In some rats, delipoidization also extended to overlying parts of the fascicular zone. This group of rats also had no sudanophobic layer. Examination of structural distinctions of the adrenal cortex of the 2d group of rats impressed us in that there was no subglomerular layer or distinct boundary between the different zones due to transformation of cells of the glomerular and reticular zones into cells of the fascicular zone, and for this reason the width of the latter increased.

Examination of the thymus of animals in the 3d group revealed signs of moderate involution in only 2 out of 8 rats, whereas distinct involution of the thymus was found in all animals of the 2d group. This was indicated by the reduction in size of the lobes, replacement of lymphoid tissue in some lobes with fibrous or fatty tissue, paucity of cortical lymphocytes, as a result of which the boundary between the cortical and medullar substance became vague, thickening of interlobular layers of connective tissue and increase in number of mast cells in them. It should be noted that involution was referable primarily to thymus lobes situated along the periphery, and only in a few instances did we also observe atrophic changes in deep-lying lobes.

The spleen of rats in the 3d group did not differ from that of the 4th group, with the exception of some increase in hemosiderin content. Submitting the rats to hypokinesia lead to hypoplasia of white lienic pulp. This was indicated by the reduction in size of lymphoid follicles, as well as number and size of their clear centers. The intensity of plasmatization and erythropoiesis in the spleen of animals in the 2d group did not change, while hemosiderin content increased to about the same extent as in the 3d group.

Analysis of the obtained data warrants the belief that when rats are placed in tight box-cages they develop an acute stress reaction which persists for the 7 experimental days, as indicated by inhibition of weight gain, delipoidization and hypertrophy of the adrenal cortex, hypoplasia of the thymus and white pulp of the spleen. "Suspending" the rats caused development of moderate and relatively brief stress, the anxiety stage of which was already over by the 7th experimental day. That there had been a stress reaction could be determined only retrospectively, on the basis of some decrease in thymus weight, insignificant adrenal hypertrophy, absence of sudanophobic zone in the adrenal cortex and accumulation in the reticular zone of the cortex of droplets of lipids. Appearance of the latter is inherent in the phase of restoration of lipid content following stress. The moderate degree of stress when experimental animals were suspended was also confirmed by the absence of inhibition of weight gain in experimental rats. Similar data, indicative of development of a moderate stress response during 7-day suspension, were also obtained in biochemical studies [5]. They revealed that ACTH, corticosterone and prolactin levels in rat plasma rose only on the 1st and 3d experimental days, whereas on the 7th day there was normalization of all tested hormones. It should be noted that, unlike the model of weightlessness developed by Ye. A. Ilyin and V. Ye. Novikov, "suspension" of rats by the Morey method [3] has a considerably greater stressogenic effect on rats. This is indicated by the decrease in body [4] and thymus [2, 6] weight, and increase in absolute weight of the adrenals [7].

Thus, a comparative morphological study of the severity of the stress reaction developing in the adrenal cortex, thymus and spleen of rats submitted to 7-day hypokinesia in box-cages and by suspension by the tail revealed that the latter has a significantly less stressogenic effect than hypokinesia of like duration. The moderate severity and relatively brief duration of the stress response to suspension are definite advantages of this model of weightlessness as compared to hypokinesia, since the effect of removing a load from the locomotor system is manifested in a purer form.

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EFFECT OF ANTIORTHOSTATIC POSITION AND DIFFERENT ILLUMINATION ON SENSITIVITY OF SKIN IN UPPER HALF OF THE BODY TO ULTRAVIOLET RADIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 20 May 86) pp 81-82

[Article by I. V. Zubkova, L. V. Gutorova and N. Ye. Panferova]

[Text] No previous studies had been made of the effect of redistribution of blood to the upper half of the body, which is inherent in weightlessness, onsensitivity of the skin to ultraviolet radiation (UVR). There is sparse and contradictory information as well concerning the effect of illumination of the skin on its sensitivity to UVR. There are data indicative of both attenuation and enhancement of UV sensitivity of the skin in daylight [1, 4]. For this reason, it is of practical interest to explore questions of the effects of antiorthostatic [head-down tilt] hypokinesia (HDT) and varying degrees of illumination on the body's capacity to perceive UVR when selecting conditions for preventive exposure of operators to UVR during spaceflights.

Methods

A total of 27 men 35 to 40 years of age participated in our study. Two series of studies were pursued with the 1st group (19 men): we tested the effect of HDT (-12°) for 2 h on UV sensitivity of the skin on the chest, abdomen, back and inner aspect of the arm; we determined the effect of mixed illumination of the skin (UVR + daylight at wavelengths above 315 nm) and illumination by UVR alone on its sensitivity to UVR. We compared the results to data obtained when testing subjects in horizontal position.

In the 2d group of subjects, we tested the effect of changing from seated to HDT position (-12°) on UV sensitivity of the skin of the chest, abdomen and back.

We used a 6-tube luminescent UVR source, the radiation dose rate from which constituted 0.035, 1.6 and 0.8 W/m^2 in the UV C (wavelength <280 nm), UV B (280-320 nm) and UV A (>320 nm) ranges, respectively. Radiation was delivered from a distance of 0.5 m to the skin surface. Angle of beam incidence was 90°.

Skin sensitivity to UVR was determined using a Tkachenko biodosimeter, which consists of a metal plate with 6 rectanbular cells and a sliding flap. The minimal amount of UVR eliciting erythema was taken as the minimal erythemic

dose (MED). Radiation dose was computed from the power of the UVR source and exposure time. Onset of erythema was determined visually. For more precise evaluation of UV erythema, it was determined by two researchers independently of one another. Means were taken when the findings did not coincide.

The entire material was submitted to statistical processing with computation of means, mean differences between paired variants, standard errors of means and values for Student's criterion.

Results and Discussion

It was established that skin sensitivity to UVR during brief (2 h) HDT increased, as compared to parameters obtained for subjects in horizontal or seated position: there was statistically reliable 10.6±1.3% decrease in MED during HDT for the skin of the chest, 10.7±1.3% decrease for the abdomen, 11.8±1.5% for the back and 18.0±0.9% decrease for the arm in subjects of the 1st group when the skin was exposed to UVR and visible light (see Table). When the skin was exposed only to UVR, MED during HDT decreased by 9.5±2.2% for the skin of the chest, 9.3±2.6 for the abdomen and 9.5±0.9% for the back.

MED for different skin regions as a function of body position and illumination conditions, mJ/cm^2 (M±m)

Illumination	Body position	Exposed region			
		chest	abdomen	back	arm
UVR + daylight	Horizontal	61,5±3,6	65,6±4,1	60,8±3,4	54,4±4,7
	HDT	55,0±2,3*	58,6±4,3*	53,6±3,4*	45,6±4,1*
UVR	Horizontal	76,0±3,6*	78,2±4,4	76,0±5,1	—
	HDT	68,8±2,3**	70,9±3,6*	68,8±4,6*	—
UVR + daylight	Seated	59,3±3,6	67,5±4,3	60,0±5,0	—
	HDT	54,0±3,6*	63,7±4,3*	53,2±5,0*	—

Note: Statistically reliable differences are given, as compared to parameters of subjects in horizontal or seated position
*p<0.05
**p<0.01

With change from seated position to HDT, MED decreased by 8.9±2.1% for the skin of the chest, 8.7±2.8% for the abdomen and 11.3±2.8% for the back.

Measurement of MED under different illumination conditions revealed that exposure to daylight enhanced skin sensitivity to UVR. In the absence of daylight, MED was higher in subjects who were in horizontal position by 23.5±2.4% for the skin of the chest, 20.6±2.4% for the abdomen and 25.0±2.2% for the back (p<0.05). Analogous findings were made in subjects during HDT: MED when the skin was exposed only to UVR was 26.0±2.2% higher for skin of the chest, 20.4±2.5% for the abdomen and 28.4±2.4% higher for the back (p<0.05).

Thus, the results of these studies revealed that there is increase in skin sensitivity to UVR during brief HDT.

It is known that formation of UV erythema is due to increased delivery of blood to superficial vessels of the skin (mainly arterioles and subpapillar venules), which are dilated under the effect of biologically active substances [2, 3]. During HDT, there is redistribution of blood from vessels of the lower half of the body to the upper half, including skin vessels. Evidently, during HDT there is a sort of summation of the effects of biologically active substances with the vasodilating effect of hydrostatic pressure. In the presence of increased blood in the skin during HDT there is manifestation of UV erythema after shorter exposure time, i.e., it requires a smaller dose of UVR. This is apparently the cause of increased sensitivity of the skin to UVR when blood is redistributed to the upper half of the body.

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DISCUSSIONS

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DISCRETE ADAPTATION TO SENSORY CONFLICT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 11 Nov 85) pp 82-86

[Article by B. I. Polyakov]

[Text] According to current conceptions, impairment of the customary forms of interaction of afferent systems--"sensory conflict"--is the principal etiological factor of motion sickness (MS), including its space form [17, 47, 50]. In essence, it consists of the fact that information about body shifts in an unusual inertial gravity environment, which comes from the vestibular and other functionally related receptor systems (optic, proprioceptive), is in contradiction with the sensory stereotype that was formed in the course of prior experience. For example, during head movements in weightlessness the semicircular canals are stimulated just like they are on earth, whereas the otolith receptors are stimulated in an unusual way, since the pulses of linear accelerations are not associated with the customary gravity vector. An analogous signal mismatch occurs in the optic-proprioceptive system, etc. The integral sensory image that arises is in contradiction to the sensory stereotype that was formed upon moving in earth-bound conditions.

The psychoneural system of probabilistic forecasting is involved in forming the response to weightlessness [15, 17, 35, 36]. The new sensory stereotype emits signals about occurrence of an improbable (unpredictable) situation, from the standpoint of individual experience, in relation to which the body does not yet have formed programs of adaptive behavior stored in memory.

Individual differences in resistance to MS are attributable to the properties of adaptive systems, including the adrenosympathetic system [2, 4, 7, 8, 11, 12, 28, 37, 39]. High activity and sufficient functional reserves of these systems constitute the condition for rapid development of adaptive processes. Otherwise, the specific program of adaptation to a new sensory stereotype does not have time to form in real time, which leads to development of non-specific forms of defense reactions, including MS.

Thus, the process of adaptation can be enhanced via several basically different pathways. One of them is activation of adaptive systems by means of pharmacological or other factors. It has been shown, for example, that use of one of the adaptogens, extract of prickly eleuterococcus, is highly effective for this purpose. The product was found to be particularly effective when

combined with passive vestibular conditioning [1]. However, in order to obtain a positive effect, long-term intake of the extract for a 3-week course is required, with subsequent conditioning period.

Pyrimidine (potassium orotate) and purine (riboxin) precursors of nucleic acid synthesis, as well as the cyclic analogue of gamma-aminobutyric acid and activator of RNA polymerase, piracetam, were used for an analogous purpose [10]. The choice of these products was due to their stimulating effect on synthesis of ribonucleic acids, which is a powerful factor of adaptation to extreme stimuli [20]. However, in this case too, a marked increase in resistance to MS was noted only with prolonged (for 7 to 14 days) intake.

Another means of alleviating the adaptation process is to lower the intensity of pathogenic effect per unit time, for example, when restricting head movement, which some cosmonauts do at the early stages of exposure to weightlessness. This delays development of acute MS symptoms at the price of slowing down the work pace and, in a number of instances, temporarily stopping work.

Finally, a third means can be proposed for alleviating the process of adaptation to sensory conflict--fractional adaptation, the principle of which is to periodically "disconnect" a subject from a given situation, just like an individual with cardiorespiratory insufficiency makes stops when going up a staircase. The advantages of such a mode of adaptation to the most diverse environmental factors are growing increasingly obvious. Thus, on the example of cold stimulation, it was shown that intermittent exposure can enhance resistance many times faster than prolonged, continuous exposure [23, 33, 34]. It has also been established that a "pulsating" mode of pressure chamber conditioning of an individual is characterized by a high antihypoxia efficacy [14], etc.

The pauses between periods of active interaction with the environment should not be simply periods of passive wakefulness. Apparently, one adapts to unusual conditions faster if periods of activity are alternated with periods of sleep.

This hypothesis is based on ideas of sleep as an active process, which is aimed at specific phases at processing information received in a waking state, restoration of emotional and autonomic equilibrium, development and consolidation of programs of adaptive behavior, in brief, at what the central nervous system (CMS) does not have time to cope with in a waking state, when primary processing of information coming from sense organs is prominent in its activity [16, 31, 40]. During sleep, "internal inputs" are of main significance; through them information is delivered that is stored in the brain--memory about the past, predictions and plans for the future [36]. It can be assumed that some important changes occur during sleep in the system of probabilistic forecasting ("fresh for the morrow").

According to one hypothesis [45], rapid sleep intensifies the function of noradrenergic neurons and serves to maintain in the CNS homeostasis of catecholamines, the role of which in providing high resistance to MS has been demonstrated [11, 12, 25, 26, 28].

Experimental studies established that, when performing complicated tasks, which required that an animal learn a basically new type of behavior for which it was not initially prepared, the probability of occurrence of rapid sleep in the first few hours after learning is proportionate to the degree of assimilation of this new situation [41, 42, 49]. Consequently, rapid sleep is needed for processing and assimilating new information that requires a creative approach [43, 44]. With total sleep deprivation for one or several nights, higher mental functions are the first to be affected--capacity for concentration of attention, orientation in a new situation and capacity to adapt to it [46]. The opinion is also held [16] that REM sleep is related to providing adaptation to various types of conflict situations.

Considering the etiopathogenetic role of "sensory conflict" in development of MS, it can be assumed that periods of controllable sleep would make it possible, so to speak, to detach oneself from "extraneous" information and gain time to form in the CNS the optimum program for control of specific adaptive reactions.

Observation of ship physicians, data obtained during spaceflights, as well as the results of some experimental studies are a practical confirmation of the desirability of such an approach. For example, it was established that sleep of adequate depth and duration can retard appreciably the onset of seasickness [38].

Electrosleep has been used with success as a means of preserving and improving efficiency of ship crews, as a means of rapid formation of a new dynamic stereotype [9].

Electrosleep combined with adaptogens of plant origin, as a means of correcting sleep disorders due to the adverse ship-board factors, was found to be more effective than autogenic training and drugs, and it is recommended as an easily controlled means of enhancing work capacity and preventing cumulative fatigue in crews [32].

A course of electrosleep is suggested to "enhance the adaptive capacities of the body in order to eliminate emotional stress and enhance mental work capacity of individuals working as traffic controllers, drivers and engaged in intense mental work" [30].

A similar method of therapeutic use of pulsed electricity--central electroanalgesia--is being used with success in many branches of clinical medicine to control the functional state (electrotranquilization) and to obtain an anesthetic effect (combined electroanesthesia). Use of electrotranquilization in sports medicine has shown the potential of this method with respect to accelerating human acclimation and enhancing adaptability at extreme temperatures, with significant change in time zone, etc. [13].

On the basis of the results of studies pursued on ships, central electroanalgesia is recommended for long voyages in order to attenuate nervous and emotional stress, enhance mental tolerance and restore autonomic equilibrium [29].

It was reported that Cosmonaut G. S. Titov, whose inflight vestibulovegetative disorders have been repeatedly described, felt considerably better after sleeping [6]. It was also shown that, following a flight aboard the Soyuz-12 spacecraft, cosmonauts presented some impairment of movement coordination, faster resting pulse, lability of blood pressure and other signs of anadaptation to earth's gravity. All these signs virtually disappeared after a night's sleep [5].

Examination of the first crew of the Skylab orbital station on the first day after their mission also revealed a number of objective and subjective symptoms of anadaptation to earth. On the first night back on earth, the astronauts slept for about 12 h, which improved their condition appreciably. In a test for resistance to MS, a station pilot showed good results, but declared that he could not have performed this test as well on the day he completed a flight, or more precisely, he could not perform it in its entirety [48].

It is remarkable that, although natural sleep, electrosleep and central electroanalgesia are different states, their effect on resistance to MS and in some variants of clinical application is analogous.

It can be assumed that inclusion of additional periods of controllable sleep or, if necessary, extending the period of natural sleep, in the work schedule of an operator would result in speedy adaptation and attenuated manifestations of MS.

The probably efficacy of such an approach is also indicated by the results of studies that revealed that central electroanalgesia was instrumental in adaptation of subjects to prolonged antiorthostatic [head-down tilt] hypokinesia, as well as in readaptation of Cosmonaut Yu. V. Romanenko to conditions on earth [24].

Finally, the results of our experimental studies [27] revealed that electropulse delivery to the CNS in the mode of electroanalgesia causes rapid increase in resistance of MS, if used in the presence of already developed vestibulovegetative disorders. Examination of 35 healthy men who submitted to a test with complex accelerations according to I. I. Bryanov [3] established that delivery of electropulses for 60 min to individuals with existing symptoms of MS improved tolerance in most cases to a second test (immediately after awakening) by an average of 76% ($p<0.01$). In a control series of tests with stimulation by electropulses, no reliable differences were demonstrated. Use of such factors for preventive purposes (before the test simulating MS) was ineffective.

Our findings were confirmed entirely by the data of other authors [21, 22], who also showed that central electroanalgesia for a 1-h pause between two successive tests simulating MS by the system of S. S. Markaryan [19] improved tolerance to the second test by a mean of 76%, as compared to the first one. Moreover, the second session of electroanalgesia virtually eliminated the adverse residual signs of MS, whereas in the control group these symptoms persisted for many hours.

Thus, a discrete mode of adaptation to sensory conflict in an unusual gravity environment, by means of having the subject "detach" himself from this

situation, for example, by means of electrosleep mode pulses, central electroanalgesia or other methods of controllable sleep, can accelerate, under certain conditions, formation of a new sensory stereotype and thereby aid in an operator's professional performance.

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CURRENT EVENTS AND INFORMATION

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SECOND ALL-UNION CONFERENCE ON PHYSIOLOGY OF EXTREME STATES AND INDIVIDUAL PROTECTION OF MAN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (manuscript received 17 Feb 87) pp 86-89

[Article by S. G. Salivon]

[Text] Implementation of the preventive approach as the basic concept of Soviet health care is inseparable from evaluation of man's health status, investigation of conditions under which he works, strain on adaptation mechanisms, mobilization of reserve capacities of the body under both ordinary environmental conditions and in the presence of extreme factors. The expanding area of human endeavor has brought to a head some ecological, sociohygienic and psychophysiological problems; it has advanced questions of physiology of extreme states and individual protection to the fore of theoretical and clinical medicine.

The problem of extreme states and deleterious working conditions is currently causing acute concern not only on the part of hygienists and physiologists, but psychologists, sociologists, industrial organizers and representatives of many clinical disciplines. This was fully reflected in the breadth and diversity of topics covered at the All-Union Conference on "Physiology of Extreme States and Individual Protection of Man," and it is indicative of the intensive work being done about these problems at institutes of the USSR Academy of Sciences, USSR Academy of Medical Sciences, institutions under the Ministry of Health, All-Union Central Trade-Union Council, specialized laboratories of other agencies and VUZ's of our country.

Prominent scientists of our country, working in 65 organizations under different ministries and agencies participated in the work of this conference, which was organized by the USSR Ministry of Health and Institute of Biophysics of the USSR Ministry of Health.

The main problems raised for discussion at the conference were concerned with the effects of adverse ambient temperatures, altered barometric pressure and toxic factors. There was discussion of psychophysiological problems of human performance under extreme conditions, methods of correcting and restoring the functional state with exposure to extreme factors, questions of individual protection of man and automation of scientific research.

In his opening remarks, L. A. BULDAKOV, corresponding member of the USSR Academy of Medical Sciences, observed that our entire nation, governed by the decisions of the 27th CPSU Congress, is experiencing an important time of restructuring, acceleration of socioeconomic development. Significant changes are also taking place in the health care area, in theoretical and clinical medicine. At the present time, one of the most important directions of scientific research is the study of the effects on public health of complex, combined and associated environmental factors, and hygienic standard-setting. Then L. A. Buldakov dwelled on the use of individual protection gear (IPG), as one of the elements in the complicated set of preventive measures aimed at assuring safe working conditions and preventing occupational diseases. Much importance is also attributed to the tactics for use and modes of use of IPG with consideration of diverse industrial, climate and occupational factors.

On behalf of headquarters of the Center for Cosmonaut Training imeni Yu. A. Gagarin, the political department and cosmonauts, the conference participants were welcomed by V. A. DZHANIBEKOV, pilot-cosmonaut of the USSR, twice awarded the title of Hero of the Soviet Union. He stressed that questions discussed at this conference cover not only traditional, "terrestrial" occupations, but pilot-cosmonauts. The entire system of training and special conditioning of cosmonauts is based on scientific developments which consider the effects of unusual spaceflight factors, stress situations, irregular and emergency conditions.

V. A. Dzhanibekov expressed hope that specialists in the field of physiology of extreme states will continue their reserach in such important directions as the effects of weightlessness and validation of steps for protection against the adverse effects of this factor, elaboration of measures to preserve physical and mental work capacity under spaceflight conditions and refinement of methods of postflight restoration of functional state of cosmonauts.

D. I. SHPARO, chief of the Polar expedition of KOMSOMOLSKAYA PRAVDA newspaper, reported on the principal achievements of many years of biomedical research pursued jointly with the Institute of Biophysics, USSR Ministry of Health, and Institute of Clinical and Experimental Medicine, Siberian Department of the USSR Academy of Medical Sciences. Special attention was devoted to analysis of the distinctions of psychophysiological states of expedition members during many-day crossings, including those made during polar night, and development of strategy and tactics of medical support of such crossings. He noted the need to create a system of individual protection for people working under self-contained conditions at high latitudes. D. I. Shparo then discussed preparations for an expedition involving cross-country skiing at the South Pole and called upon specialists in extreme physiology and individual protection to participate actively in the biomedical research program.

Papers were delivered at plenary sessions of the conference that dealth with a number of high-priority directions of development of Soviet medicine. V. S. KOSHCHEYEV (Institute of Biophysics--IBF--USSR Ministry of Health), corresponding member of the USSR Academy of Medical Sciences, dwelled on important problems of individual protection under extreme ambient conditions, stressing the importance of developing the methodology for constructing systems of individual human protection, evaluation and prediction of their reliability and efficacy.

The potentials of concrete approaches to validate guidelines and strategy in selecting means of individual protection as applied to performance under concrete extreme conditions were demonstrated; the need was stressed for development of a national system of individual human protection under extreme conditions. The paper of ZINCHENKO (USSR Academy of Pedagogic Sciences), corresponding member of the USSR Academy of Pedagogic Sciences, discussed the attitude of modern man to the numerous flows of information, organization of volume and content of information, its selective perception and the individual attitude of a specific person to its content. Extensive experimental material was submitted, which indicated the link between work load, qualifications and certain other socioindustrial characteristics, on the one hand, with onset of somatic disorders and other functional disturbances, on the other.

The problem-oriented paper of Professor F. B. BEREZIN (First Moscow Medical Institute imeni I. M. Sechenov) dealt with emotional stress, personality distinctions and defense mechanisms. In particular, he discussed in detail the mechanisms of psychological adaptation. This author makes a distinction between three closely interrelated aspects of mental adaptation: actually mental, sociopsychological and psychophysiological. Such a division is based on comprehensive investigation of psychodiagnostic parameters, level of cerebral activity, vegetohumoral regulation and other data characterizing activation of physiological functions during work. The formed multicomponent structures of mental adaptation have an effect, in many respects, on the nature of the emotional stress response and neurovegetative stability in these individuals, on their health and performance.

The paper of A. V. VALDMAN (Institute of Pharmacology, USSR Academy of Medical Sciences) discussed important questions of pharmacological correction of extreme states. Emotional stress is the first phase of development of any extreme state. The author cites data concerning mechanisms of action of different classes of neurotropic and psychotropic agents, effects on formation of behavioral, physiological and biochemical elements of emotional stress; he discusses the role of emotional stress in development of specific changes in the body that occur under the effect of different environmental factors; he stresses the role of individual typological distinctions of responses to a stressor and administration of a drug. In the opinion of Professor N. N. VASILEVSKIY (Institute of Clinical and Experimental Medicine, USSR Academy of Medical Sciences), parameters of flexibility, stability and coherence of physiological processes should serve as the basis of identifying individual typological differences in people, predicting adaptation to extreme conditions and correcting deadaptation disorders. These parameters are tested by means of methods using biological feedback. A distinction is made between groups of individuals with low, average and high adaptability. On the basis of the same methods with feedback, the author developed means of correcting deadaptation disorders by conditioning for stability of functional biorhythms and coherence of physiological systems.

V. G. VOLOVICH (Institute of Biomedical Problems--IMBP), doctor of medical sciences, dwelled on the complicated problems of human survival during self-contained existence in uninhabited regions of the North, tayga, desert, aquatoria of seas and oceans. He stressed that people who abruptly find

themselves in such regions (as a result of accident, disaster or other causes) often perish due to ignorance and inability to behave under these conditions, due to a lack of volitional effort to fight for preservation of life and health, lack of gear and protective equipment, rather than because of the excessive extreme factors. In his opinion, it is imperative to offer practical training, comprehensive instruction for all individuals who move from civilized cities to a rigorous environment, to which most of the public is not adapted and in which they always overestimate their capacities.

The work of the section dealing with extreme factors in aviation and cosmonautics concentrated on three main directions: investigation of the effect of altitude factors on the body, in particular, decompression disorders in man; long-term exposure to accelerations and means of anti-G protection; effect of simulated weightlessness on various functions, particularly in individuals of older age groups.

General interest was inspired by the paper of V. I. CHADOV and L. R. ISEYEV (IBF, USSR Ministry of Health), which dealt with maximum allowable coefficient of oversaturation (MACO) as a function of postdecompression pressure. On the basis of vast experimental material, these authors established the safe modes of decompression which virtually correspond to MACO of 1.63 in the altitude range of 6100-9300 m, while further increase in "altitude" to 10,800 m causes it to decline. New data were reported by L. G. GOLOVKIN et al. in a paper dealing with the use of the principle of blood distribution in designing altitude gear, and the paper of V. P. KATUNTSEV et al. (IMBP, USSR Ministry of Health) entitled "Ultrasonic Demonstration of Gas Bubbles and Appearance of Caisson Disease Symptoms in Man During Ascents to High Altitudes." In the paper of YU. S. ILYUSHIN, A. S. YAROV, and V. S. YAKOVLENKO (IBF, USSR Ministry of Health), it was shown that use of high-modulus materials that expand in one direction in a pressure suit provides for high mobility and convenience in working, in spite of presence of excess pressure.

In a series of papers dealing with simulation of weightlessness, much attention was devoted to prevention of functional disturbances, in particular by means of physical conditioning. These recommendations were summarized in the paper of V. I. STEPANTSOV and I. B. KOZLOVSKAYA (IMBP, USSR Ministry of Health). The authors demonstrated that retention of skills and capacities for performance of work at specified speed provides the necessary orthostatic stability and tolerance to accelerations for the entire period of antiorthostatic [head-down tilt] hypokinesia.

Some interesting scientific data were reported concerning hemodynamics during hypokinesia and immersion (T. A. KRUPINA and L. A. FOTINA, IMBP, USSR Ministry of Health), changes in cerebral circulation and endocrine status under the effect of lower body negative pressure (R. A. TIGRANYAN et al., Scientific Research Institute of Standardization and Control of Drugs, USSR Ministry of Health). Among the papers dealing with methodology, much interest was displayed in the report of V. YE. ZAYCHIK et al. (Scientific Research Institute of Medical Radiology, USSR Academy of Medical Sciences) concerning the feasibility of intact demonstration of calcium and other element levels in the human body by means of complex radiometric equipment--methods of neutron-activation analysis.

At section meetings dealing with extreme physical and chemical environmental factors, papers were discussed that dealt with physiology of extreme states in man at high and low temperatures, hygienic aspects of improving standards for industrial microclimate, guidelines for development and tactics for use of individual protection systems (IPS; L. G. ARUTYUNYAN et al., Scientific Research Institute of General Hygiene and Occupational Diseases, USSR Academy of Medical Sciences; G. V. BAVRO et al., IBF USSR Ministry of Health; R. F. AFANASYEVA, Scientific Research Institute of Industrial Hygiene and Occupational Diseases, USSR Academy of Medical Sciences, and others). Much attention was devoted to questions of combined and complex effects of toxic agents, the combined effect of chemical and physical factors, as well as the role of the immune system in adaptation to chemical factors in the industrial environment (V.V. KUSTOV et al., IBF, USSR Ministry of Health; V. T. MAZAYEV et al., First Moscow Medical Institute imeni I. M. Sechenov; B. T. TULEBEKOV, Institute of Physiology and Experimental Pathology at High Altitudes, Kirghiz Academy of Sciences, and others).

During the work of the section entitled "Correction and Restoration of Man's Functional State With Exposure to Extreme Factors," there was discussion of a wide range of questions dealing with the ways and means of correcting functional states when man is exposed to extreme factors, assessing their efficacy, mechanisms of action of different means of correction.

The papers of P. P. DENISENKO (Leningrad Medical Institute) and S. S. LOSEV (Scientific Research Institute of Toxicology, USSR Ministry of Health) dealt with general basic questions of selection of protective pharmacological agents against various extreme factors. It was noted that protective pharmacological agents at the present time consist only of many components that affect nervous, neuroendocrine regulation and metabolic processes. It was also stressed in these papers that the problem of pharmacological protection against extreme factors has two very distinct aspects--preventive and therapeutic--and this must also be borne in mind when development new protective pharmacological agents.

Much interest was displayed in questions of using nondrug methods of correction and enhancement of work capacity of individuals exposed to adverse conditions. In the summary paper of V. I. ILYIN (First Moscow Medical Institute imeni I. M. Sechenov), there was a general classification of nondrug individual protection against extreme factors: prophylaxis, preventive correction, autocorrection, rehabilitation. It was noted that development of remote physical factors is one of the most promising directions in the development of new drug IPG.

Several papers discussed the question of controlling man's functional capacities by different methods and means—reflexotherapeutic (A. M. VASILENKO, Central Scientific Research Institute of Reflexotherapy, USSR Ministry of Health; A. M. KARPUKHINA, I. A. CHAYCHENKO et al., Scientific Research Institute of Psychology, Ukrainian Ministry of Education), psychotherapeutic (I. N. KALINAUSKAS et al., Scientific Research Institute of Psychology, Ukrainian Ministry of Education; L. S. SOLNTSEVA et al., All-Union Scientific Research Institute of Physical Culture), physiotherapeutic (K. V. SUDAKOV et al., Institute of Normal Physiology imeni P. K. Anokhin). The problem of combined use of nondrug means of correcting man's functional state was discussed in the

paper of V. S. CHUGUNOV et al. (Neurosis Clinic imeni Z. P. Solovyev). It noted the important role of examining the adrenosympathetic system in planning combined therapy for individuals characterized by psychoemotional stress.

Discussion of questions of automating biomedical studies of man's state under extreme conditions held a prominent place at the conference.

The recommendations offered at the conference stressed the need for continuing research on physiology of extreme states and individual protection of man, special attention being given to validation of the informativeness of parameters and criteria for assessing physical and mental work capacity of man under extreme conditions, ongoing diagnostication and physiological mechanisms of immediate and long-term adaptation of man to extreme factors, forecasting functional states and protecting man against extreme factors and neuropsychological stressors, pscyhophysiological aspects of human resistance and adaptation to adverse factors and searching for the means of retaining efficiency and enhancing resistance under such conditions, evaluation and correction of any possible long-term sequelae of exposure to extreme factors, validation of wise approaches to development of highly effective and physiologically acceptable systems and means of individual protection.

ANNIVERSARIES

UDC: 612+612.275.1]:92 Mirrakhimov

MIRSAID MIRKHAMIDOVICH MIRRAKHIMOV (SIXTIETH BIRTHDAY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, Sep-Oct 87 (signed to press 18 Aug 87) pp 89-90

[Article]

[Text] Professor Mirsaid Mirkhamidovich Mirrakhov, outstanding physiologist-clinician, corresponding member of the USSR Academy of Medical Sciences, academician of the Kirghiz Academy of Sciences, honored physician and honored scientist of that republic, director of the Kirghiz Scientific Research Institute of Cardiology, celebrated his 60th birthday on 27 March 1987.

Having graduated with distinction from the Kirghiz Medical Institute in 1948 and successfully defending his candidatorial dissertation in 1952, M. M. Mirrakhimov devoted his entire life to internal medicine and clinical physiology.

His works in the field of clinical physiology brought wide renown to M. M. Mirrakhimov as a scientist. He was the first to formulate the thesis of phasic nature of the process of individual adaptation to high-altitude hypoxia.

The many years of collaboration between the Problem Laboratory for "Physiology and Pathology of Man At High Altitudes," headed by M. M. Mirrakhimov, and the Institute of Biomedical Problems (N. A. Agadzhanyan) resulted in elaboration of guidelines for screening people to work under extreme environmental conditions, including space. It was shown that altitude adaptation enhances significantly human resistance to diverse deleterious factors (hypoxia, temperature, etc.) and augments the body's reserves. The results of these studies served as the basis for a number of collections, monographs, candidatorial and doctoral dissertations (V. I. Korolkov et al.). M. M. Mirrakhimov is a brilliant clinician and pedagogue. He prepared 11 doctors and 46 candidates of sciences.

This scientist has authored 417 scientific works, including 20 monographs. About 40 articles and surveys were published in the foreign press. Such books as "Essays on the Effects of the Mountain Climate of Central Asia on the Body" (1964), "Mountains and Constitutional Resistance" (in collaboration with N. A. Agadzhanyan, 1970), "Heart Disease and the Mountains" (1971), "Treatment of Internal Diseases With Mountain Climate: (1977), "Mountain Medicine" (in collaboration with P. N. Goldborg, 1978) and "High-Altitude Cardiology" (in

collaboration with T. S. Meymanaliyev, 1984) became textbooks for clinical physicians working in the high-mountain regions of our country. He has written some of the chapters in a multivolume manual of physiology published by the USSR Academy of Sciences.

In recognition of his scientific merits, M. M. Mirrakhimov was elected corresponding member of the USSR Academy of Medical Sciences (1969) and academician of the Kirghiz Academy of Sciences (1974). The USSR State Prize and, twice, the Kirghiz State Prize were bestowed upon him.

A communist and patriot of his homeland, M. M. Mirrakhimov worthily represented Soviet medical science abroad. He participated in the work of the 15th International Congress on Aviation and Space Medicine (Prague, 1966), the General Assembly of the International Biological Program (Seattle, 1972), 26th Congress of International Physiological Science (New Delhi, 1974), European Congress of Cardiologists (Antwerp, 1976; Paris, 1980), meeting of WHO (Geneva, 1982) and International Congress on Internal Medicine (Kyoto, 1984). He was elected member of the International Association of Human Biology.

M. M. Mirrakhimov is head of the Scientific Medical Council of the Kirghiz Ministry of Health, member of the presidiums of the Scientific Medical Council of the USSR Ministry of Health, Kirghiz Academy of Sciences, member of a number of All-Union Scientific Problem Commissions, deputy chairman of the All-Union Society of Cardiologists, member of the presidium of the All-Union Society of Internists, Rheumatologists and Nephrologists, Scientific Council for Cardiovascular Disease of the USSR Academy of Medical Sciences and chairman of Kirghiz societies of internists and cardiologists. He is a member of the editorial board of the journals, FIZIOLOGIYA CHELOVEKA [Human Physiology] and ZDRAVOOKHRANENIYE KIRGIZII [Kirghiz Public Health], and of the editorial council of several clinical and physiological journals. As chairman of the medical section of the Kirghiz society, Znaniye, he wages active propaganda of medical information amoung the public, and for this received the N. I. Vavilov medal (1985).

M. M. Mirrakhimov is a member of the Central Committee of the Kirghiz Communist Party and deputy to the Supreme Soviet of Kirghiz SSR. The orders of Lenin, October Revolution, two decorations (1961, 1971), medals, etc., have been bestowed upon him.

The editorial board, coworkers and numerous disciples of M. M. Mirrakhimov cordially congratulate him on his noteworthy birthday, wishing him good health and further success in the field of Soviet medical science and public health care.

OBITUARIES

UDC: 612+612.76]:92 Kakurin

LEONID IVANOVICH KAKURIN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (signed to press 18 Aug 87) pp 90-91

[Article by Editorial Board]

[Text] Leonid Ivanovich Kakurin, department head at the Institute of Biomedical Problems, USSR Ministry of Health, doctor of medical sciences, professor, recipient of the USSR State Prize and Honored Scientist of the RSFSR, died suddenly early this year.

Upon graduating from the Military Medical Academy imeni S. M. Kirov, L. I. Kakurin worked in military units [chasti] in the capacity of junior physician, and later, chief of the surgical department.

In 1954, L. I. Kakurin was transferred to research work.

In 1969, L. I. Kakurin defended his doctoral dissertation, entitled "Effect of Limited Muscular Activity on Man," and in 1971 the title of professor was conferred upon him. L. I. Kakurin was a diversified researcher and organizer of scientific research, and he is definitely to be credited with the choice and implementation of the most promising and practically important directions of investigation. For over 10 years, L. I. Kakurin was the scientific administrator of combined investigations that required involvement of many scientific research teams.

He was one of the first in our country to validate the need for investigation of functional distinctions of the human body when muscular activity is limited (hypokinesia). Subsequent multilevel work in this field, which was performed in our country, made it possible to establish a new and promising teaching on human hypokinesia in medical science.

The gratitude of administrators of institutions, agencies and the USSR Ministry of Health was repeatedly expressed to him for his direct participation in organizing medical support of mission programs aboard Vostok, Soyuz and Salyut spacecraft.

L. I. Kakurin has authored more than 150 scientific works. Eleven candidatorial and three doctoral dissertations were prepared and successfully defended under

his scientific guidance. He was the titular editor of the monograph, "Spaceflights Aboard Soyuz Series Craft," in which the results of investigations of the main problems of medical support of crews were summarized.

Professor L. I. Kakurin was a member of the joint Soviet-American working group for space biology and medicine. L. I. Kakurin and the teams of the laboratories that he headed made a large contribution to theory and practice of space medicine in the development of problems of validation and construction of systems of medical monitoring of crews in flight, validation of methods and means of protecting man against deleterious flight factors, adaptation and functional capacities of man when his active muscular activity is restricted.

L. I. Kakurin enjoyed deserved authority among a wide circle of space researchers. He devoted much effort and skill to the solution of the most important problems of space medicine, and he has trained a large number of highly qualified specialists.

In November 1978, the USSR State Prize was awarded for the investigation of Professor L. I. Kakurin et al., "A Cycle of Studies Dealing With Medical Validation and Introduction of Ways and Means of Preventing the Adverse Effects of Weightlessness on Man, Which Made it Possible to Perform Long-Term Manned Spaceflights in the Soviet Union."

The scientific research section that L. I. Kakurin was a team of Communist Labor. Communist L. I. Kakurin pursued much public and scientific work, being a member of two scientific councils, member of the examination board, propagandist of the Frunze CPSU Republic Committee, head of a seminar in the network of party education and chairman of the board of preceptors.

L. I. Kakurin devoted much attention to dissemination and popularization of scientific advances. His data have been published in the newspapers, PRAVDA, IZVESTIYA, SOVETSKAYA ROSSIYA and TRUD.

A participant in the Great Patriotic War, L. I. Kakurin was the recipient of three Orders of the Red Star and medals.

For his many years of scientific, industrial and public endeavors, by ukase of the Presidium of the RSFSR Supreme Soviet, the honorary title of Honored Scientists of the RSFSR was bestowed upon L. I. Kakurin in 1982.

A bright memory of L. I. Kakurin, scientist, administrator, pedagogue and preceptor, will remain forever in our hearts.

UDC: 629.78:612.014.47:92 Leverett

IN MEMORIAM: S. D. LEVERETT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (signed to press 18 Aug 87) pp 91-92

[Article by Editorial Board]

[Text] Sidney D. Leverett, editor of the journal, AVIATION, SPACE AND ENVIRONMENTAL MEDICINE, died on 3 March 1987 after a lengthy and serious illness.

Sidney D. Leverett was appointed editor in November 1980 at the recommendation of the executive board of the U. S. Aerospace Medical Association. He successfully administered the editorial board for 6 years, being instrumental in disseminating highly qualified scientific information on important problems of aerospace medicine. He retired in December 1986 for health reasons.

Dr Sidney D. Leverett was born in 1926 in Houston (Texas). He received his higher education at the University of Texas. He received his doctorate in philosophy in 1960.

From 1944 to 1980, Dr Sidney D. Leverett served in the U. S. Air Force. His scientific and practical interests were concentrated in such areas as physiology of the cardiovascular system, gravity physiology, development of antigravity gear and decompression. He has authored 65 scientific works dealing with aerospace medicine, as well as chapters in 3 books.

For many years, Dr S. D. Leverett delivered lectures for specialists working in various branches of aviation and space medicine.

In 1978, at the invitation of teh USSR Academy of Sciences, Dr S. D. Leverett came to the Soviet Union and delivered lectures at scientific research institutes in Moscow and Leningrad.

Dr Sidney D. Leverett is an active member of the Association of Specialists in Aerospace Medicine, member of the International Academy of Aerospace Medicine. In 1973, he served as president of the department of biomedical research and biomedical engineering of the U. S. Aerospace Medical Association; in 1975, he was president of the Aerospace Physiological Society.

He has repeatedly been the recipient of high prizes of different U. S. agencies and and organizations for his fruitful scientific, organizational and public endeavors.

While editor of AVIATION, SPACE AND ENVIRONMENTAL MEDICINE, Dr Sidney D. Leverett was instrumental in the working collaboration with our journal, KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA. In 1984, appendixes were published to both these journals, with his participation and collaboration, which dealt with the results of research done by Soviet and American authors on important problems of space biology and medicine.

The editorial board of this journal expresses its profound sympathy to members of the U. S. Aerospace Medical Association and to the editorial board of the journal that Sidney D. Leverett headed so fruitfully for many years, as well as to his family.

BIBLIOGRAPHIC REFERENCE BOOK DEALING WITH BIOMEDICAL AND SOCIOPSYCHOLOGICAL PROBLEMS OF SPACE EXPLORATION AND OTHERS BEING READIED FOR PUBLICATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (signed to press 18 Aug 87) p 92

[Announcement]

[Text] "Biomedical and Sociopsychological Problems of Exploration of Space and Regions of Worth With Extreme Living Conditions (Bibliography)"--1988 (first quarter), 25 sheets, 1.50 rubles.

This book sums up information on the entire set of problems of aerospace biology and medicine in 1982-1983. The guide constitutes an in-depth retrospective analysis of periodicals, monographs, as well as proceedings of symposiums and conferences, published in the USSR and abroad.

In this book, there is an exceptionally comprehensive rubrication of material, and a significant number of systematized and annotated works. The inclusion of an author index and system of references and footnotes permits multiclassification of works dealing with multilevel studies.

This bibliography includes information about experimental basic and theoretical research that is inseparable from the solution to a wide range of biomedical problems of space exploration.

The book will be of interest to a wide range of scientists--chemists, physicists, biologists, physicians and psychologists specializing in biomedical and sociopsychological problems of adaptation to extreme conditions.

The size of the printing will be determined by the number of requests for this book, to be sent to: Scientific Library, 123007, Moscow, Khoroshevskoye sh., #76a.

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Institute of Biomedical Problems

SYNOPSES OF ARTICLES FILED WITH THE ALL-UNION SCIENTIFIC RESEARCH INSTITUTE OF MEDICAL AND MEDICOTECHNICAL INFORMATION AND ALL-UNION INSTITUTE OF SCIENTIFIC AND TECHNICAL INFORMATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 5, Sep-Oct 87 (signed to press 18 Aug 87) pp 93-96

UDC: 612.13+616.12/14.092

PHASIC CHANGES IN HUMAN CARDIOVASCULAR SYSTEM PARAMETERS AFTER CHANGE FROM HORIZONTAL TO VERTICAL POSITION

[Synopsis of article by Sh. T. Avetikian, G. G. Khramova and D. V. Gusarova]

[Text] Pulse in arteries of the head, arm and lower leg (by rheography), pulse of common carotid artery (piezoelectric sensor), photoplethysmogram of the finger and rheocardiogram were taken in 18 essentially healthy men who submitted twice to an active orthostatic test, in baseline recumbent position and for the first minutes of orthostatic position. From the rheocardiogram, we determined systolic cardiac output (SCO), arterial pressure (BP) was monitored according to lag of pulse wave (LPW) in the finger as related to the rheocardiogram. It was found that, at the start of the orthostatic test, heart rate (HR) increased in two steps (A and B phases, 6.0±0.3 and 11.3±0.4 s, respectively, was the duration of these phases) to a maximum that different from the baseline by 34.7/min, then following a period of relative slowing (C phase) it reached a stable level that exceeded the baseline by 18.8/min. SCO, on the contrary, at first diminished to a minimum in the B phase then, after relative increase in the C phase, stabilized at below the baseline in an analogous fashion (in steps). The amplitude of arterial pulse in all tested regions (with the exception of the head and, in part, the arm) virtually echoed the SCO changes. The amplitude of the rheogram of the head increased by 70.7% in the A phase, then gradually diminished to baseline values by the 2d min of the test. There was analogous change in LPW time, indicating that BP was below the levels inherent in orthostasis during A and B phases, reaching them only in the C phase. Thus, phasic changes in functional organization of the circulatory system of organs have been delineated at the start of the orthostatic test. The A phase, in which a 20.8% decline of SCO was noted with a compensatory increase by 26.9/min in HR, was characterized by substantial decrease in tonus of arteries in the upper part of the body (to the greatest extent those of the head), which was aimed at maintaining blood flow in organs when cardiac output is diminished and BP is low. At the B phase, further

decrease in SCO elicited even greater rise of HR and decline of amplitudes of arterial pulse in all tested regions, reaching 53.2% in the lower leg. The tonus of arteries of the head and arm is diminished in this phase, BP did not reach the level required for orthostatic position. At the C phase, which betan after 11 s of the test, the circulatory system changed to a mode close to that of stable orthostasis. BP rose and tonus of arteries in all tested regions increased, with decrease in HR. But the typical feature of the C phase was presence of signs of over-regulation marked by higher values for SCO than in subseuqent periods and greater amplitude of pulse in all arteries, as well as relative orthostatic bradycardia. By the 2d min of the test, all parameters reached levels inherent in stable orthostasis. 1 illustration, 19 references.

UDC: 616.12-073.97-073.584

SPECTRAL ANALYSIS OF CARDIAC INTERVALOGRAM ENVELOPE

[Synopsis of article by Ya. Z. Grinberg]

[Text] Analysis is made of a model of the heart's conduction system, and it is shown that the sequence of R waves can be described in the form of a frequency-modulated pulsed signal (FMPS). Consequently, for spectral analysis one cannot use the standard methods of spectral analysis, for example, Fourier's discrete transform (FDT), the method of Blackman-Tyuki or others that are oriented toward uniform digitization of information.

There is discussion of procedures that eliminate ambiguity in interpretation of the results of spectral analysis, which is related to description of the RR interval series as a function of an ordinal number.

Formation of the envelope of a cardiac intervalogram is a process of converting FMPS into an amplitude-modulated pulsed signal, the distinctive feature of which is nonuniformity of appearance of readings. In this case, for spectral analysis one should use procedures of the least-squares method (LSM). Here, harmonic functions are independent variables in the model. Use of LSM is not limited by the requirement of uniform quantization of information. For real-time systems and in order to use computer memory conservatively, use of reucurrent LSM is examined. Correction of parameters of the spectral model is then made in the time between access of successive R waves.

The second procedure is based on spectral breakdown of FMPS. The low-frequency part of the FMPS spectrum is, in this instance, the sought spectrum of the envelope of the cardiointervalogram. To run the procedure, the initial sequence is converted into pulses with finite duration of 1 ms. The obtain signal is viewed as an analogue signal and it is digitized by means of readings delivered uniformly every 1 ms. The digitized signal is processed by means of FDT. When a run lasts 200 s, the frequency of the first harmonic is 0.005 Hz. When the top frequency of the cardiac intervalogram envelop is 0.4 Hz, it is sufficient to scan the first 80 harmonics. The pulsed nature of the signal in question reduces significantly the volume of computations required for FDT. 2 illustrations, 7 references.

UDC: 612.014.426

MECHANISM OF RESPONSE OF ADRENOMEDULLARY SYSTEM TO STATIONARY HIGH-INTENSITY MAGNETIC FIELDS

[Synopsis of article by L. D. Klimovskaya and L. V. Kokoreva]

[Text] The objective of this work was to determine the role of the central nervous system (CNS) in mechanisms of activation of the medullary layer of the adrenals elicited by a stationary magnetic field (SMF) with high intensity. This study was conducted on 174 white rats. After 24-h adaptation to the surroundings, the animals were exposed to total-body SMF in a vertical direction with induction of 0.4 T for 3 h. Control rats were kept in the same room under identical conditions for the same period of time. Immediately after exposure to SMF, experimental and control animals were decapitated. Epinephrine (E) and norepinephrine (NE) levels in blood and adrenals were measured by a fluorimetric method. E concentration in rat blood constituted 6.98±0.69 μg/ℓ. After 3-h exposure of animals to SMF of 0.4 T this parameter rose to 10.75±0.99 μg/ℓ ($p<0.02$). SMF also elicited an increase in adrenal epinephrine, with retention of level of its precursor, NE. Nembutal (60 μg/kg), hexenal (100 μg/kg) and aminazine (10-20 μg/kg) were used to depress CNS function; they were injected intraperitoneally before exposure to SMF to experimental rats and, concurrently, to control animals. After injection of these agents, SMF did not cause reliable change in blood E concentration. In the presence of barbiturates, there remained a mild tendency toward increase in blood A content in experimental rats: the differences between experiment and control constituted ±1.35 μg/ℓ after giving nembutal and +1.07 μg/ℓ after hexenal. The similarity of effects of both barbiturates, of which only nembutal had a marked peripheral ganglioblocking effect, is indicative of a central mechanism of depression of SMF effect. Aminazine had the most marked blocking action on the effect of SMF: after its administration blood E concentration was lower in experimental rats (4.83±0.41 μg/ℓ) than controls (5.64±0.92 μg/ℓ). This agent was used in the testing of the adrenals. Administration of aminazine prevented intensification of hormonopoiesis in the adrenal medulla under the effect of SMF. Blocking of the response of the adrenomedullary system to SMF with prior administration of aminazine is perhaps related to its properties as a central adrenolytic. The results of these studies revealed that, in the presence of depression of CNS function, SMF ceases to have a stimulating effect on activity of the adrenal medulla. The obtained data indicate that the effect of SMF on the adrenomedullary system is mediated and manifested through the involvement of higher branches of the CNS. 1 table, 1 illustration, 12 references.

UDC: 612.176-087

MORPHOMETRIC EVALUATION OF CARDIAC CHANGES IN EXPERIMENTAL ANIMALS UNDER THE EFFECT OF STATIC PHYSICAL LOADS

[Synopsis of article by M. S. Gnatyuk]

[Text] There is contradictory information in the literature concerning hypertrophy of the myocardium with regular physical exercise; there is no agreement

about the morphological and functional changes in the hypertrophied heart. The distinctions of structural alteration of myocardial regions under the effect of static loads have not been sufficiently studied.

In this work, the hearts of 36 white female Wistar rats, which were submitted to moderate and intensive static loads, and the hearts of 12 control animals were studied using a set of morphometric methods, including organometry (separate weighing of different parts of the heart, planimetry of endocardial surfaces of its chambers), histosterometry (measurement of diameter of cardiomyocytes and their nuclei, nucleus-cytoplasm and stroma-parenchyma ratios), morphological-statistical and informational analysis (calculation of entropy, relative entropy and superfluousness) and the usual histological methods.

It was established that static physical loads elicit appreciable structural change in compartments of the myocardium, mainly with prevalence of a hypertrophic process in the right ventricle. In order to examine the heart with hypertrophy, which developed with moderate static loads, morphometric, information and histological methods were used, and no morphological damage to its different compartments was demonstrable. The cardiac hypertrophy demonstrated on the tissular and cellular levels was balanced, proportionate in nature. Under such conditions, the myocardium can cope for a long time with the increasing hyperfunction.

Intensive static physical loads elicit not only hypertrophy of the right ventricular myocardium, but appreciable functional and morphological disturbances in this region, which are demonstrable on all levels of structural organization of the heart. Concomitant lack of order and disorganization of morphofunctional systems of the heart and pathohistological damage to its compartments, as well as negative extracardiac factors associated with increasing hyperfunction, can lead to disruption of compensatory and adaptive processes, as well as appearance of insufficiently hypertrophied heart. 2 tables, 20 references.

UDC: 612.824.014.47

CHANGES IN CEREBRAL HEMODYNAMICS IN ANTIORTHOSTATIC POSTION AS A RESULT OF REFLEX FACTORS

[Synopsis of article by A. M. Vasilenko, V. I. Bannaya, T. F. Filina and A. F. Zubarev]

[Text] The effect of electropuncture (EP) on hemodynamic reactions in antiorthostatic (HDT) position with -15° tilt angle was studied on nine healthy subjects. The rheoencephalogram (REG) was recorded in the masto-mastoidal (MML) and fronto-mastoidal (FML) leads. Subjective sensations related to HDT were assessed using the principle of a visual analogue scale.

EP prior to HDT prevented the typical dramatic increase in amplitude and change in form of the rheographic wave. In the first minutes of HDT, in control tests, the rheographic index increased by a mean of 210% in the MML and 150% in the FML. In studies with use of EP, the increment in these parameters did not exceed 47 and 45%, respectively. There was appreciable inhibition and

attenuation of development of subjective sensations of discomfort that are typical of HDT. The preventive effect of EP lasted for 2.5-3 h. Repetition of the procedure was associated with slowing of build-up of symptoms and easier tolerance to the factor to the end of a 6-h test.

An effective procedure of preventive electropuncture against circulatory changes with HDT was selected on the basis of severity of responses of systemic and cerebral hemodynamics. The most distinct preventive effect was obtained with EP of the collar zone and auricular concha.

The changes in dicrotic (DCI) and diastolic (DSI) indexes under the effect of EP were a function of individual responses to HDT. While significant (more than 50% of baseline) increase in DCI and DSI was observed in control tests, they diminished with EP. Insignification deviations of indexes in the control HDT were also associated with minor change under the effect of EP.

Rheographic testing of the lungs and lower leg, performed concurrently with REG, revealed that the EP effect occurs not only through reflex influence on tonus of cerebral vessels, but increase in delivery of blood to internal organs and lower extremities. This adaptive response, which was mild in the control tests, is enhanced with EP.

EP modulates natural adaptive mechanisms of controlling vascular tonus and cardiac function, providing for fuller use of individual potential set of adaptive reactions with HDT. Current conceptions of the physiological essence of EP, the methodological advantages of this method and available technical capabilities to implement it enable us to recommend it as a promising preventive agent in the period of preflight training of cosmonauts, during flights and in postflight rehabilitation. 4 illustrations, 12 references.

UDC: 612:51.001.57

THEORETICAL ANALYSIS OF SOME PHYSIOLOGICAL MECHANISMS OF HUMAN TOLERANCE TO HEAD-PELVIS GRAVITATIONAL ACCELERATIONS

[Synopsis of article by R. D. Grigoryan]

[Text] A study was pursued on a mathematical model of hemodynamics in order to validate limited compensatory capacities of arterial baroreceptor regulators of hemodynamics and to analyze the physiological mechanisms of human circulatory tolerance to linearly increasing +Gz accelerations. In addition to additively acting sinocarotid and aortic baroreflexes, a generalized pressor reaction was included in the circuit of hemodynamic control in the model, which is manifested when accelerations are in excess of about 3 G, and it increases with increase in accelerations.

The studies were pursued on a model of a three-dimensional human cardiovascular system for seated position. It was assumed that the direction of the gravity vector and longitudinal axis of the trunk coincide. Three series of model experiments were performed: with open chain of central reflex regulators; with inclusion of only the circuit of arterial baroreflexes and, finally, with consideration of the generalized pressor reaction.

It was shown that the resistive-capacitive properties of vessels and heterometric and homeometric self-regulating mechanisms of the heart have a substantially limited compensatory reserve in the presence of linearly increasing +Gz accelerations. The tolerance limit, as assessed by perfusion blood pressure at eye level, constituted only 1.8 G, with a gradient of build-up of 0.5 G/s and 2.3 G with a gradient of 0.1 G/s. Thus, it was proven that central reflex regulators are mandatory participants in implementation of circulatory homeostasis with exposure to accelerations.

The capabilities of aortic and sinocarotid baroreflexes were also found to be limited. Inclusion of this circuit could not provide for the known range of tolerance to longitudinal accelerations, even with simulated use of an anti-G suit, since these reflexes changed from synergistic to antagonistic at a certain time, when pressure in the aorta exceeded the baseline. In order to have heart rate and vascular tonus continue to increase and counteract the diminished blood flow and pressure in the aorta when +Gz exceeds about 4 G, an additional reflex is needed to suppress the inhibitory effect of the aortic depressor reflex. This thesis is validated by appropriate calculations. It is assumed that a generalized pressor reaction unrelated to cerebral ischemia or an emotional factor, but of a mechanoreceptor nature could serve as such a reflex. Modeling revealed that this reaction must present typical dynamics: it is activated after initial activation of baroreflexes, the effectiveness of which diminishes when accelerations exceed 3 G. The typical dynamics of activation of baroreflexes and generalized pressor reaction spread over time determines the dynamics of increase in heart rate, which has three periods: initial and final rapid rise with intermediate slowing within the range of 2-4 G accelerations. There is also discussion of the physiological mechanism of raising the limit of tolerance to +Gz gravity accelerations by means of breathing under excess pressure. In addition to a purely mechanical protective effect of creating a pressure "head" for vessels of the head, as the protective effect of this procedure is usually explained, it also involves reflex mechanisms. The latter consist in essence of the fact that rise in extravascular thoracic pressure limits inhibitory afferentation of mechanoreceptors in the walls of these vessels, thereby causing increase in the overall pressor effect. 1 illustration, 16 references.

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